A COURSE OF LECTURES

ON

GENERAL PATHOLOGY.

GENERAL PATHOLOGY,

AS CONDUCIVE TO

THE ESTABLISHMENT OF RATIONAL PRINCIPLES FOR
THE DIAGNOSIS AND TREATMENT
OF DISEASE;

A COURSE OF LECTURES,

DELIVERED AT ST. THOMAS'S HOSPITAL,

DURING THE SUMMER SESSION OF 1850.

BY

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TO

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PROFESSOR OF ANATOMY AT THE ROYAL ACADEMY,
ETC. ETC. ETC.

THIS VOLUME IS INSCRIBED:—

THE GRATEFUL AND AFFECTIONATE HOMAGE

OF A PUPIL TO HIS MASTER;

THE TRIBUTE

OF HABITUAL REVERENCE FOR HIS GENIUS AND HIS VIRTUES;

THE ACKNOWLEDGMENT OF LIFE-LONG OBLIGATION

TO HIS TEACHING, TO HIS EXAMPLE, AND TO HIS FRIENDSHIP.

ADVERTISEMENT.

The following Volume contains a short Course of Lectures in General Pathology, which has recently appeared in the columns of the *Lancet*.

It is now submitted to the profession in a separate form, with such further correction and extension as the Author's other engagements have allowed him to make during its reprint.

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A COURSE OF LECTURES

IN

GENERAL PATHOLOGY.

INTRODUCTORY LECTURE.

Definition of Pathology as a Science; its dependence on anatomical, chemical, and clinical observations; its relation to Physiology; Disease, what? prevalence of exterior causation in producing it; symptoms and products of disease are determined by types of healthy structure and function; reaction; arrest or excess of development; norma of disease; query as to disease essentially independent of exterior cause; hereditary developmental diseases; spontaneous declensions of type? influence of Pathology in improving treatment of disease; pleasures and rewards of the study.

Gentlemen: In approaching the frontier of a new country, we naturally desire to possess some previous general information as to the objects which will fall beneath our notice; and thus you, to-day, on the threshold of another study, may reasonably expect to be informed by me as to its subject-matter, and limits, and relations.

Pathology (πάθους λόγος, the discourse of whatsoever is suffered) etymologically implies *the Science of Disease.* In inquiring with you at some length in what sense these two words (*science* and *disease*) are, or ought to be, used in the definition just given, I believe that I may best fulfil the explanatory objects of an introductory lecture.

Hereafter, I shall have something to say of the word *disease;* meanwhile, I will take for granted that each of you attaches a familiar meaning to the word; and in that sense, for the moment, I will leave it.

The other word, *science*, is always in our mouths; let us ask with what definite meaning it is used.

If we distinguish an infinite diversity in the objects of sense—if our eyes acquaint us with a thousand grades and combinations of colour—if our palates discriminate manifold differences of taste and flavour—if our ears inform us variously of the pitch and rhythm of sounds—if, through the same or other inlets of sense, we are enabled to recognize the several degrees of cohesion, of weight, of magnitude,

of duration, of number—do we extend the name of *science* to these sensuous impressions, or to the involuntary comparisons (cognitions of similitude and difference) which arise in them? No. Or again, if we have certain record or personal memory that, during a given period of time, night has followed day, winter has followed summer, sleep has followed waking, death has followed life, do we give the name of *science* to this experience of succession? No. These impressions and recollections constitute only the raw material which presently, and in a very altered form, becomes incorporated into the structure of *science;* representing the food (if I may say so) of a future organism, the stones of a future architecture, the chaos of a future kosmos.

That which essentially marks the operations of *science* is, the reduction of an infinite exterior diversity into systems and formulæ expressive of mutual relation. In other words, *science* consists in the intellectual apprehension of whatsoever is objective in nature—in its apprehension, namely, according to certain specific necessities of the human intellect, which oblige us, in proportion as we are human, to search for *laws and conditions of manifestation*, wherever the senses observe progressive development, or distinct succession, or quantitative differences or degrees; to search for *the essential*, wherever there is a complexus of impressions; for the *causative*, wherever there is a sequence of phenomena; for the *principal of order* or classification, wherever there is plurality of existence.

To apprehend the phenomena of nature—not in their crude and concrete state, but analyzed, compared, interpreted, divested of accidental complication, and stated in their abstract forms, or in their generalities of mutual connection; to apprehend their laws of manifestation—not as mere empirical memories of what has been, but as the means for confident prediction of what will be; to apprehend classification—not as a mere trick of numerical notation, but according to the types or essential characters of things;—these are the acts of science.

See, for instance, out of the innumerable variety of phenomena which we now refer to gravitation,—the weight of what is lifted, the velocity of what falls, the solidity of one object and the fluidity of another, from astronomical observations, from suggestions apparently so far asunder as the dropping of an apple, or the rounding of a dew-drop, and the measured sweeping of the planets; see, out of this heterogeneous crowd of sensuous impressions, how the single essential function has been educed by the matchless sagacity of Newton, as the centripetal tendency of matter; and see again how, in recognizing the essential identity of phenomena so various, he likewise assigned their law or condition of manifestation with a completeness and simplicity quite unequalled in science: "the particles of matter attract each other with forces directly proportional to their masses, and inversely proportional to the squares of their distances." Or observe, again, out of how many quantitative phenomena in chemistry, at first sight of little import or with little connection, a law, of scarcely less magnitude than that of gravitation, has been developed by the genius of

modern science, showing that the whole system of chemical combination is according to a numerical scale, in which every element and every union of elements has its possibilities of combination limited and defined in respect of every other element, or every other union of elements.

In respect of the studies which are peculiar to our own profession —those which relate to organized beings, there is the same distinction to be drawn between the mere perception or registration of phenomena, and their reduction to a scientific form; in these, as in other departments of knowledge, you will find that the description of particular phenomena does not in itself constitute science.

[Illustrations were given by comparison of Descriptive Anatomy with Physiology.]

If now you pass to the study of Pathology, understanding what it must be to constitute a science legitimately so called, you will observe that it professes to interpret and systematize the phenomena furnished by the body in disease—phenomena, the primary recognition of which has arisen in the auxiliary and anterior labours of the morbid anatomist, the morbid chemist, and the clinical observer; it constitutes, in fact, the rational element (as distinguished from the mere exercise of eyesight, hearing, touch, &c.) in the science of medical observation.

While I distinguish Pathology from the passive exercise of the senses in matters of medical experience, and while I tell you that it constitutes the rational element in the science of medical observation, pray do not fall into the grievous error of thinking, even for a moment, that the pathologist can fitly refrain from observation, or can do otherwise than observe incessantly and critically; much less that he can throw himself on the resources of his own intellect, as means of progress independent of observation.

I wish you indeed to feel that, in order to make the best use of your senses, you must employ something more than those senses—that, in order to scientific observation, you must react on every exterior impression with an intellectual purpose and energy of your own. I would caution you, certainly, against being mere sight-seers in the dead-house, or mere crepitation-counters in the ward; but at least equally I would warn you against any endeavour to divorce experience from your reflections, and against any belief that theory, apart from observation, can furnish you with aught better than shifting sands for the foundation of your knowledge. The merest observer may possibly (though, as I think, insufficiently) collect his materials without being a pathologist. He may describe a red mucous membrane, a hard lung, a big heart, a heavy bone, an opaque lens, a quick pulse, a vomiting or a purging, a cutaneous eruption, a contracted pupil, a paroxysm of ague or of epilepsy, a crystalline deposit from the urine, or a microscopical congeries of cells; he may describe any of these actions or phenomena without the slightest knowledge of their method of production, or of the laws which govern their existence. But the converse does not hold good; no progress can be made in pathology except from the ground of accurate and

extensive observation; and any endeavour to establish it on another foundation, or to spin it forth from the devices of one's imagination, cannot but prove impotent and fruitless.

Two years ago, I availed myself of the opportunity offered by my commencing connection with this School, to explain at length what I conceived to be the true method of pathological study;* and I endeavoured, on that occasion, to illustrate the manner and the proportion in which the mind and the senses must co-operate (or rather, in which the senses must follow the guidance of the intellect) for the purposes of scientific investigation. Therefore, I refrain from dwelling at present on this subject, and pass to other points, relating rather to the limits and affinities of the science.

The phenomena with which the pathologist has to deal are (as I have already mentioned to you) those which occur in the ancillary studies of morbid anatomy, morbid chemistry, and clinical observation; and it is almost superfluous for me to tell you, that these studies presuppose a knowledge of health. All the phrases of pathological observation imply that knowledge as their standard. When you say, handling an organ,—brain or lung,—that it is hard or soft, or very hard or very soft, you mean that the brain is soft as compared with healthy brain, the lung dense as compared with healthy lung. When you say that a man's pulse is quick, or that his pupil is contracted, you mean quick as compared with a healthy man's pulse, contracted as compared with a healthy man's pupil, under similar circumstances. When you say that colocynth is a purge, or morphia a narcotic, you mean that a healthy man would discharge more feces, or have more sleep, under the influence of these drugs than if left to himself—and so on.

What, then, you may ask, is the relation of Pathology to Physiology? When the latter word is used in its true (which is also its largest) sense, it includes the former; it implies, namely, the total science of life, whether in health or in disease. In common conversation, however, "physiology" is often restricted to denote only the science of life in health; and it is then used in direct contradistinction from "pathology," as the science of life in disease.

No doubt it is convenient for some purposes, that there should be a division of labour in these subjects; that some men should devote themselves especially to observe and explain the phenomena of the healthy body,—others especially to the task of unfolding the more intricate mysteries of disease; but, gentlemen, whether you consider pathology to be a part of physiology in the act of its application to medicine, or whether you view it as a separate study standing in contrast to physiology, in either case let me impress on you that the science is really one, the method of observation and research one, and that any supposed science of disease must of necessity be crude or fictitious, unless it be a direct deduction from the knowledge of health. Your observations will be utterly valueless, if you do not

* On the Aims and Philosophic Method of Pathological Research: An Inaugural Address, delivered at St. Thomas's Hospital. London, 1848.

uniformly and consciously start from this standard: your knowledge of healthy anatomy must precede your power of observing morbid anatomy; your knowledge of healthy function must precede your power of noting the morbid functions or symptoms of disease; your knowledge of healthy chemistry in the body must precede your power of detecting what is wrong in the chemical products of disease; your knowledge of all that is quantitative or rhythmical in the healthy body must precede your power of recognizing those changes of increase or diminution, of acceleration or retardation in its phenomena, which occur either in disease, or under the influence of medicines.

Further, in every case of disease coming under our care, physiology dictates those questions and observations which are, or ought to be, prior to any attempt at opinion or treatment. By enabling us to decide what are the essential characters (as distinguished from the accidental complications) of disease, by telling us what several combinations of symptoms may concur with the one first obvious to us, and what different signification would belong to each of such combinations, it establishes our means of rational diagnosis, fixes the degrees of our approximation to certitude, and exposes the frivolity of medical guesswork.

It would be easy for me to multiply examples of the manner in which the pathologist deals physiologically with such facts and phenomena as are supplied to him, by observations at the bedside, or in the dead-house; but one or two obvious instances will sufficiently serve to illustrate to you the course usually taken by the mind in such investigations.

[The following instances were here dwelt upon: pathological inquiry into hypertrophy of the heart, as founded on the general laws of muscular growth and development—pathological inquiry into albuminuria, as founded on an insight into the mechanism of the circulation, the structure of glands, and the process of secretion—pathological inquiry into neuralgia, as founded on the physiological conditions of nervous convection and sympathy.]

Now, gentlemen, let me beg your attention to another view of the subject. When, in commencing my lecture, I spoke of pathology as the science of *disease*, I said that I should presently say something on the latter word. What, then, do we mean by the word *disease?* for as yet I have left it to your own general impression and prejudgment, and perhaps you are hardly prepared to believe that there can be any difficulty in the definition. On examination, however, you will find that it does involve considerable difficulty.

Your definition of *disease* would probably take this direction: "Nature" (you would say) "gives a certain habit and method of working to the body—a certain law or *norma* of action; any departure from this *norma*—anything *abnormal* in the actions of the body, constitutes disease."

Now, let us try this definition with a case: A man has a tumour in the orbit; it grows larger and larger, displaces the globe of his eye and blinds him; or perhaps it originates in the globe of the eye itself, and presently inflammatory enlargement of the globe comes

on, which continues with great suffering till the organ bursts and is spoiled; and, on examination, you find that all this serious mischief depends on the presence of a parasitic animal (an hydatid), which has by some unknown means been introduced from without, and has acted as a foreign irritant in exciting all the consequences of inflammation. Or the same development of hydatids may take place in an internal organ, the liver, for instance, where, eventually, it not only spoils the organ, but terminates life. Or you may take a case of scabies, where a minute parasitic insect is seen burrowing in the skin, and producing vesicular eruption; or a case of porrigo, where a parasitic vegetable is being extensively developed on the surface of the skin, producing irritation and ulceration there. Consider, I say, any one of these cases, and you will see that the only really abnormal thing is the presence of the parasitic organism, which is not an act of the suffering body, but the act of another living body; for when the irritating parasite is there, of course it is strictly normal and healthy, that the surrounding parts should be affected by its irritation: otherwise we should require a living body insusceptible of exterior impressions and sensations. Take another case: A man has a sudden and severe pain in some part of the surface of his body, accompanied by a rush of blood to the painful spot, and by a disposition to the pouring out of serum there. This, obviously, is not a condition of health. But, if you knew that a quantity of boiling water had just been dashed on the part, you would be disposed to transfer the term *unhealthy* from the effect to the cause—from the man to the kettle. In fact, the man would have been unhealthy if this redness and vesication had not occurred. And you will find in most, or, I think, in all, the instances of inflammation, or vascular reaction, which you can adduce, that there may be made a similar objection to the use of the word *disease* in the sense assigned to it.

Or (to examine a few more cases) you see a man lying in a state of insensibility from which he cannot be roused by any stimulus or pain. Nothing, apparently, can be less normal; but, you find that he has had a blow on the head with a brick; you find a bit of bone knocked in on his brain; you lift up the bit of bone, and, directly its pressure is removed, the unhealthy state ceases. It would, indeed, have been abnormal if the brain had acted healthily under this pressure.

Or you learn that the man had previously shown symptoms indicating excitement of the brain, probably of its different parts in succession, which has gradually given place to the comatose insensibility in which you find him; but the man has been drinking poison—alcohol or laudanum, and still, you observe, the disease is not his abnormality, but abnormality of circumstances.

Or you find that for the last four days he has made but a few spoonfuls of bloody urine, and you know that he has a narcotic poison in his blood, (one, indeed, not bought at the druggist's, but quite as fatal as opium,) one formed by his own organization; you know that

the urea, which his kidneys ought to eliminate, is being retained in the system—is poisoning and killing the man.

Now, what I wish to notice in these several instances (and I might adduce hundreds more) is this: the symptoms, if you take them quite apart from the circumstances which produced them, would be abnormal; but, when you know the whole case, you are obliged to admit that, according to the normal constitution of the body, the symptoms in question ought to have followed the operation of those several causes; that the man would have been abnormal if these results had not arisen: if he could have received a dash of boiling water without the occurrence of erythema; or if his brain could have continued to discharge its functions, when oppressed with mechanical injury, or when poisoned with laudanum, alcohol, or urea.

Thus you will see that the true *norma*, or method of working, of the body embraces a variety of manifestations which practically we include in our list of diseases; and so definite and constant are those modifications of vital action which occur under variations of exterior circumstances, that we are enabled artificially to produce such modifications; and, in fact, it may be stated that medical treatment consists almost entirely in the artificial production of phenomena, which, considered apart from their causation, would be named disease.

Two patients, for instance, shall be side by side in a ward, making many quarts of urine per diem, six times their normal quantity. You go to No. 1; you find sugar in his urine; you call his symptom a disease—diabetes; its proximate cause being that he makes this vast quantity of urine because a highly diuretic material has entered his blood from the intestinal canal, and, according to the normal function of the kidney, must be eliminated with a certain proportion of water. You go to No. 2; profuse urine as before; but in this case, perhaps, reeking of turpentine, which (like the sugar in the previous instance) has been absorbed from the intestinal canal, and has stimulated this man's kidneys, as the sugar did those of his neighbour. The only difference between the two cases, as regards the phenomena of diuresis, is, that in the latter case you have got the diuretic from the apothecary's shop, and have given it perhaps to cure a dropsy; while in the former case the diuretic (sugar) has accumulated in the blood, as the product of a peculiar error of assimilation.

You will gradually find, gentlemen, that considerations like the preceding lead to a clearer view of the relations of our science. Any attempted line of demarcation between physiology and pathology soon melts away; the healthy and delightful rush of blood to the surface of the body, as we emerge from the cold bath, depends on the same apparatus and the same adaptation, as determine the still greater glow—the painful redness and effusion of serum, when boiling water, or the poison of erysipelas, is the provocant; and if we were to proceed no farther in the subject, we should be prepared to modify the definition of disease with which we started, and to speak of pathology as the *study of life under abnormal exterior relations*. But again, as we go on, a doubt arises on the absolute accuracy of this definition; whether, namely, all diseases (I mean, of course, all primary diseases)

are *exopathic*—are *affections of the body from without;* or whether some may arise in such a manner as to be called *autopathic*—may be actual caprices and spontaneities of life without any exterior causation whatsoever.

In proceeding to criticize this matter, let us first inquire generally what are the actions of the living body? The digestion of food, the formation of secretions, the absorption of chyle, the development of blood, the construction of tissues, the reception of sensations, the excitement of muscular contractions, voluntary and involuntary—all these, and many others, may briefly and generally be taken under two heads, as representing the purposes and possibilities of life: (1.) The living body in health has the power, which I have already in part illustrated to you, and which I may shortly call the power of reaction—namely, the faculty (total and also partial, with, and also without, consciousness) of receiving impressions through sensitive nerves, and responding through nerves which excite contraction, voluntary or involuntary, in the muscles of animal life, and in those of organic life, including the heart and arteries. (2.) The living body in health has the power of maintaining its own construction, according to a certain definite essential type of shape, of texture, and of chemical constitution. You have a *type of shape* for every partible segment of the body; a type for the hand, for the face, for the brain, for the larynx, for the intestinal canal, for the leg; you have a *type of texture* for the intimate structure of organs, for nerve, for cartilage, for bone, for epithelium; *a type of chemical* construction for the blood, for the bile, for the urine, for the sweat.

Now let us consider how disease operates in respect of these two spheres of function. In respect, then, first, of the morbid manifestations of excitability and reaction, as they occur in the nervous, vascular, and muscular systems (including of course, spasm, convulsion, determination of blood, and increase of secretions), we find nothing but the normal phenomena of direct or reflected excitement, varying in intensity according to the degree of stimulation. The morbid phenomena are modifications of the healthy ones, by excess, or by deficiency; we are quite certain, that, in an infinite majority of cases, this excess or deficiency of reaction depends on the excess or deficiency of stimulus relatively to the nervous centre; that it has its distinct objective cause, and is relatively exopathic.

Next, in respect of the organizing or *constructive* acts of the living body, the manifestations of disease, so far as we have exact knowledge of them, are as definite as the types of health, and, for the most part, admit of being distinctly recognized as instances of a mere excessive or defective fulfilment of those original types. Growth and development may go beyond their wonted degree, or may stop short of it in various deformities and abortions of structure; but all such apparent disorder of organization seems in reality to run in a single line or series—to represent, as it were, the upper or lower stages of a scheme of development which includes the typical construction as its most perfect manifestation. Take, for instance, those congenital deformities of the heart, which you know as the causes of cyanosis;

they do not consist in the adoption of any new type of construction; they are constructed in the normal type, but development was arrested too soon, and the design left incomplete. So with hare-lip, epispadias, spina bifida, and many like disorders, which consist in an incomplete junction of the two halves of the body; the materials of construction were normally laid down in the embryo, their type of development was normal, but the power of growth failed too soon, and left the opposite elements separated by a gaping fissure. You never see these fissures disposed fortuitously in the fœtus; you do not see them on the limbs, or set transversely on the trunk; they only occur where the embryo was originally cloven, and they represent those original clefts surviving by a defect of development. In diseases or transformations of texture, (though I can only hastily allude to them,) you see the same invariable reference to the type of construction, and the same tendency, under disturbing influences, to produce abortive approximations to it. In the growth of epithelium, especially where its renewal is disordered by the effects of mechanical irritation, and in all the products of inflammatory action, there are good opportunities of watching these phenomena of arrested and modified development; while, as an instance of excessive development, still in accordance with the original type and laws of growth, take the transformation with old age of various permanent cartilages into bone, this transformation being in the line of normal development, but a step in excess of that in which it should have remained stationary.

Disease, then, in its first form (so far as we know it) seems likely, for the most part, to consist merely in something more or less than health; in some excess or deficiency, not in actual diversity or opposition; and this quantitative error may relate either to the *completion of a material type* (as the ingredient of organic and humoral diseases); or it may relate to the *proportions of impression and excitement* (as the essence of functional diseases). Now this mere "more or less," in the process of growth, or in the phenomena of excitement—this mere excess or deficiency in some *act*, or in some *product* of the body—would, at first sight, almost of necessity, appear a result of exterior causation; for we can conceive an infinite variety of outward influences relating to nourishment, temperature, and casual stimuli, which must exert a constant quantitative control over the functions alluded to.

There are, however, some forms of disease, for which it seems difficult, or almost impossible, in the present state of our knowledge, to discover any theory, or at least any evidence, of exterior causation. Cases of congenital deformity—though they obviously consist, for the most part, in defective or excessive fulfilment of a normal type, cannot always be traced satisfactorily to any such origin. There are some which are as yet inexplicable. Still more difficult are those morbid diatheses, or constitutional diseases, of which scrofula, cancer, and gout, are examples. These may, almost with certainty, be spoken of as hereditary peculiarities of blood-development, perhaps facilitated by circumstances, but not easily (if at all)

producible by artificial means. Not only are we unable distinctly to refer these disorders to exterior causation; but we are likewise unable, with our present knowledge, to fix (relatively to the healthy constitution and development of the blood) what are the precise conditions in which the diatheses consist. We see their peculiarities (especially that of the scrofulous diathesis) transmitted by hereditary succession, almost like the distinctions of race which mark a Negro, a Chinese, or a Caucasian; and it is a matter of the utmost interest in pathology, as well as one of great difficulty, to determine with certainty whether these diatheses ought to be considered as aboriginal variations of development, inseparable from the existence of the individual, and constituting him (so to speak) a *variety* of man, with a peculiar type of chemical development; or whether, on the other hand, any diathesis which he may exhibit should be regarded as a mere modification of degree, higher or lower, in his chemical development? and if so, whether such developmental excess or deficiency should be referred to the influence of exterior circumstances, as an *exopathic* phenomenon, or to an immediate primary dependence on the vital power of the individual, as an *autopathic* phenomenon?

In endeavouring to form an opinion on this subject, I cannot but feel that extreme doubt hangs over it, and renders it for the present impossible to give a complete philosophical definition of disease. A large majority of cases would no doubt admit of being described as the *normal phenomena of life under abnormal circumstances;* but in respect of other (chiefly developmental) diseases, it may be doubted if this description would apply; or whether, rather, we must not recognize an actual abnormality in the acts of life—recognize (that is to say) a primary dynamical affection of Life, under the influence of which the several vital manifestations become liable to faulty development, by excess, by declension, or by variety.

The discussion through which I have just led you may serve to illustrate a remark which has often been made with respect to definitions,—that a matter admits of philosophical definition only when its investigation has been completed; not, as some imagine, at the commencement, and on the threshold of inquiry. And accordingly, while we may describe Pathology to consist in the *Science of Life under other conditions than those of ideal perfection*, we are obliged to reserve a doubt whether the imperfect conditions in question may universally be referred to *exterior causation*, or may partly be considered as *spontaneous tendencies*, inherent in the vital principle of the individual.

Gentlemen, I ought hardly to conclude without a word or two as to the advantages which have followed, or may be expected to follow, the study of Pathology. Is Practice founded on Pathology more successful than such as is blindly empirical? Will you cure more sickness—will you save more lives hereafter, by working at Pathology now? These plain and practical questions you may rightly ask; and I can answer them without difficulty. Undoubtedly Practice is

successful in proportion as it is based on Pathology;—undoubtedly you will save more lives, and relieve more suffering, by striving diligently and constantly to establish your principles of treatment on this scientific foundation.

For the primary forms of disease—forms to be encountered and conquered by the action of direct specific antidotes, I may confess that as yet Pathology has done little. In discoveries of this nature, the empiricism of six thousand years has achieved more than the new science, which even now is but in its infancy; but, if accident has revealed, and if experience has confirmed for us, a knowledge of the properties of quinine, of mercury, of colchicum, of antimony, I cannot doubt that even these great results of popular observation will be transcended and eclipsed by the positive results of rational pathology;—that cancer, gout, and scrofula will presently yield to philosophical investigation what they have refused to blundering quackery; and that, within the lifetime of many here, there will be a specific treatment of each diathesis, founded on an exact knowledge of the physiological laws of its manifestation.

But, from this, which Pathology may do and will do, I turn to what it has done. Think, gentlemen, of the immense *negative* results which it daily achieves—of the vast amount of injurious treatment which has given way, and daily is giving way, under its auspices. You, who are at all familiar with the history of practical medicine, look back a score of years: think of the treatment of fever, of erysipelas; think how many died of venesection, how many of mercury; think of the division of nerves for central neuralgia; think of the treatment of syphilis; of the confusion of inflammation with atrophy of the brain; of the bleeding and opium in tetanus; of the inflamed kidneys irreparably damaged by diuretics; think of the treatment of heart-diseases, and of the extreme zeal with which the Physician strove against the curative tendency of Nature; think how one man's whole *materia medica* was blue-pill and black-dose; while another practitioner would hide his want of a definite object by accumulating, in a single prescription, half the heavy titles of the pharmacopœia; and, not least among the services which Pathology has rendered to mankind, observe the incalculable good it has done, with regard to very many humoral disorders and local derangements of nutrition, in going beyond the notion of a "peccant humour" as something to be purged out, and in pointing to the constitutional conditions of anæmia and depression, in which such errors of assimilation so generally arise.

In all these respects, where Pathology has been the reforming and rationalizing principle of medicine, the advantages derived from it have been immense, as counteracting mischievous practice, and as teaching us to refrain from doing harm; and I contend that the science of pathology would do more good, would save more lives, than all the vaunted specifics of empirical medicine, if only by that humble precept which it constantly impresses on the student—to be content with doing nothing when ignorant how to do good.

Thus far I have alluded only to the utilities of the science—only

to its influence in making you better practitioners, and in conducing to the cure of your patients. This is indeed a matter of the utmost importance; for, with the limited time allotted to medical education, you can surely not afford to bestow any considerable share of your industry on speculative subjects remote from useful application. Therefore is it, that I have been anxious to assure you of its extreme fruitfulness in practical results.

But yet I would not willingly suffer you to believe that the whole worth and dignity of the science consist merely in its applicability and usefulness. It has other praises beyond these. In every pursuit that can claim to be called philosophical, the labourer has his reward in the progressive solution of doubt, and in the perception of infinite details bound together in some simple and harmonious scheme. "Accustomed (says Sir John Herschel) to trace the operation of general causes, and the exemplification of general laws, in circumstances where the uninformed and uninquiring eye perceives neither novelty nor beauty, the votary of science walks in the midst of wonders; every object which falls in his way elucidates some principle, affords some instruction, and impresses him with a sense of harmony and order. Nor is it a mere passive pleasure which is thus communicated. A thousand questions are continually arising in his mind, a thousand subjects of inquiry presenting themselves, which keep his faculties in constant exercise, and his thoughts perpetually on the wing; so that lassitude is excluded from his life, and that craving after artificial excitement and dissipation of mind which leads so many into frivolous, unworthy, and destructive pursuits, is altogether eradicated from his bosom."

No science with which I am acquainted offers these mental rewards to its cultivator in so large a measure as that under our consideration. Day by day, as progress is made in its arduous and intricate problems, the student rises to a fuller appreciation of the harmony and mutual fitness of the universe. At first view, the phenomena of disease might appear to be the blind workings of chance, or the cruel strivings of an evil principle bent on marring the beautiful perfections of Nature. We see pain and misery, deformity, loathsomeness, and pestilence; every apparent form of physical evil, every apparent contrariety and caprice. We are involuntarily reminded of our great poet's lazar-house, with the innumerable shapes of anguish which it displayed:—

> Sight so deform what heart of rock could long
> Dry-eyed behold?

Intolerable, indeed, would be the spectacle, if we had no power to interpret and explain it; or if, in spite of inquiry, it still stood in our contemplation casting its long shadow over the universe, as so much necessary unmitigated evil, or as the indiscriminate operation of some wanton curse.

Our examination rewards itself by showing us far otherwise. We find that disease works according to laws definite, constant, invariable; we find in it no contradiction to the laws of life; on the con-

trary, that the latter, in their simplicity and comprehensiveness, include and account for it; that the power of adaptation to circumstances, the power of resistance to casualties, the power of repair after injury, would not be possible or conceivable attributes of the human body, except under conditions which impose the liability to disease. At every turn of the subject, and in every fresh illustration which new study reveals to us, we derive deeper and more steadfast convictions of the total absence of caprice, chance, or irregularity, even in the strangest influences of disease. We become habitual observers of that mystery which most of all tends to chasten and to elevate the mind—observers, namely, of the unbroken uniformity which prevails in the operation of Natural Laws. Standing, in the daily exercise of our profession, amidst an apparent chaos of darkness and suffering, where at first all seems, as of yore, to be "without form and void," it is our great privilege, that, by the aid of scientific insight, we are raised to a recognition of the "Spirit which moves upon the face of the waters," and which now, as in the first morning of creation, resolves that chaos into harmonious order, that darkness into intelligible light, that suffering into the feeble counterpoise of some greater and more extensive good.

Nor is this our only privilege in the philosophical study of Pathology. Living in the contemplation of Nature; contrasting our restricted faculties with her infinite empire; feeling the proportionate littleness of individual existence; and yet noting, too, that every existence, as part of a great system, lives and dies, rises and is merged, only in obedience to those harmonious laws which govern the immeasurable whole—so that, except in conformity with these laws, "not even a sparrow falleth to the ground;"—learning all this, and learning it reverently; acquiring deep convictions of our own dependence on the operation of laws which are beyond our control, and yet of the unchanging stability and comprehensiveness of those laws: we may convert these intellectual convictions into the means of moral teaching for ourselves, and may at length for our reward acquire that happy union of composure and humility which is the best gain of the Philosopher.

LECTURE II.

Blood in disease; not simply a chemical study; physiological analysis, distinguishing elements of blood according to their station in its development—whether mature, progressive, or regressive; similar principle in classifying morbid phenomena—viz.: 1. Diseased conditions arising in morbid ingestion; common poisons; limitations to their power of infecting the blood; morbid poisons; foreign bodies, cancer cells, pus.—2. Diseased conditions arising in errors of excretion; (*a*) Retention of what ought to be excreted; carbonic acid, bile, urea. (*b*) Drain of what ought to be retained; effects of diabetes, cholera, hemorrhage, serous discharges, and parasitic animal growths; secondary results of inspissation and attenuation of the blood.

GENTLEMEN: I propose devoting the present lecture to a consideration of the blood in disease. It is neither my business nor my intention to say much about the healthy condition of that fluid. I may safely take for granted that, in the Physiological Lectures, you have acquired the information which will enable you with facility to follow such details as I have now to offer you on the chief morbid affections of the blood. On the diagram-board, you see a table* from which you can refresh your memory on the particulars of its composition in health; and I will very briefly recal to you the physiological points which it is most important you should recollect.

In a person whose growth is stationary, the quantity of food passing into the body in a given time is exactly equivalent to the quantity of matter passing away in various excretions; the daily six pounds, more or less, of meat, bread, coffee, fish, wine, salad, condiments, water, &c., exactly correspond to the quantity of feces, urine, sweat, expired carbon, &c. A certain small proportion of these matters passes quite unaltered through the stomach and intestines; appearing at one terminus of the canal in exactly the same form as it entered at the other; but nearly all the substances taken into the stomach undergo solution there, or in the duodenum, are absorbed into the circulation, and make their re-appearance eventually in some new combination, in which few or none of their original properties survive. Leaving out of account that small proportion which, as I have said, passes unchanged through the canals, (such as the woody matter of vegetables, indigestible bits of smoked meat, &c.,) it may be said that the true excreta correspond exactly to what is absorbed from the food. Food, I need hardly tell you, is not taken for the sake of the excreta, or in order to furnish them; it is taken to renew the body; and, unless it were supplied to the system in considerable excess, none of it would pass into an excretion till after having entered into the construction of the body—till after having been part of some one tissue or another.

The blood, as it circulates, gives to each organ the means of repairing itself; first, by furnishing it with material of new growth;

* The table alluded to is on the following page.

secondly, by washing away from it, in a dissolved state, whatever elements of its tissue have become worn out and useless. Thus, *e. g.*, with the brain: the carotid artery carries blood to that organ; the jugular vein carries it back; and therefore, theoretically speaking, there must be this difference between the contents of the two vessels—that the blood of the jugular vein will be destitute, comparatively, of the materials necessary for renovation of the brain, (the phosphorus, the fat, &c.,) and will contain, instead of them, the effete products or waste of the brain, formed in the progress of its function,—chiefly perhaps consisting of carbonic acid, the phosphates, water, and other oxidized elements of its constitution; and then, as a final result of this process, the blood which has traversed the brain, and undergone the change in question, presently goes to other organs—organs of excretion, such as the lungs or kidneys,

* *Analysis of the Composition of Healthy Venous Blood.*

Composition of 1000 parts of healthy venous blood, according to the following authorities.	Corpuscles.	Water.	Fibrin.	Albumen.	Fat, with Extractive Matter.	Salts.
Lecanu	127	790	3	72		8
Becquerel and Rodier:						
In Males.	141.1	779	2.2	69.4	8.4	
In Females	127.2	791.1	2.2	70 5	9	
Popp	120	790	2.5	88		
Zimmermann	127	—	3.	80		
Simon:						
In Males	112.2	791.9	2.0	75.6	16.6	
In Females	106.0	798.6	2.2	77.6	12.6	
Christison:						
In Males	153.5	756.2	5.2	85.3		
In Females	120.7	795.2	2.5	81.6		
Hittorf, in Females	126.4	793.0	1.4	67.4	11.5	

Contents of 1000 parts of liquor sanguinis, deduced from the above.	Water.	Fibrin.	Albumen.	Extractive Matters, and Fat.	Salts.
According to Lecanu	904.9	3.4	82.5		9.2
" Becquerel and Rodier: .					
" In Males . . .	907	2 6	80.4	9 8	
" In Females. . .	906.4	2.5	80.8	10.3	
" Popp	897.2	2.8	100		
" Zimmermann . . .	904.4	3.6	92		
" Simon:					
" In Males . . .	894	2.3	86	18	
" In Females . . .	897	2.6	87	14	
" Christison:					
" In Males . . .	892	6.2	100		
" In Females . . .	904	2.9	93		
" Hittorf, in Females. .	908	1.6	77	13	

where the phosphates and carbonic acid get eliminated from the system.

If this were the whole history of the blood, its investigation in disease would be comparatively easy. But a chief difficulty in the study is this; that the blood undergoes changes of its own—undergoes what I can hardly call anything else than a process of growth. In addition to receiving new matter from the food, and old matter from the tissues,—in addition to feeding the several organs, and supplying the several excretions of the body, it does also itself undergo, as I have said, progressive changes of its own, analogous to the growth of the solid tissues. For the new materials which are derived to it from the food are not *blood* at the time of their addition; they are crude, immature products, which subsequently ripen within the stream of the circulation, under the influence of the maturer blood, and conformably to its composition. To some of you, perhaps, the view here suggested, of the blood undergoing development akin to growth, may be new and strange. There is an early prejudice, which makes us consider solidity of structure an indispensable preliminary for the residence and manifestation of life. Still, in spite of that prejudice, and in spite of the fluidity of the blood, you may safely believe that that red fluid is a living, growing mass; that the process of blood-formation is not the mere infusion of certain ready-made materials from without, but is as truly a process of growth as the development of cartilage or muscle.

If the power of resisting change—if the power of converting things to its own type, and perpetuating its own constitution—be signs of life in an element or portion of the body, I know none which possesses these qualities in a higher, if in so high, a degree as the blood. And further, in recalling its anatomy, you will be confirmed in this view. You will remember that, in all other elements of the body, the abundance of cell-development which you meet with, measures the activity and constancy of growth; and if you put a drop of blood under the microscope, and compare it with a patch of equal size of liver, or of brain, you are at once enabled to judge how immeasurably greater is the developmental activity in the blood; or if you look at a drop of fluid from the thoracic duct, you observe myriads of cell-germs there—germs which it is the chief, and perhaps the only, object of the lacteal and lymphatic systems to provide, and which attain their maturity, and fulfil their purpose, only when received into the blood.

And not only does the blood live and grow; but, in the mature animal, its life and growth must precede all other life and growth in the body; for first *it* grows, next other organs grow at its expense.

What I have said will suggest to you, how many liabilities to disease are included in the circumstances to which the blood is exposed; how easily morbid ingesta may become commingled with it as causes of change; how easily matters may be retained in it, which various distant organs ought to eliminate; how easily its own progressive development may be interfered with, arrested, or deranged.

The enumeration, too, that I have given of its functions in health, will show you sufficiently what particular difficulties belong to any investigation of its changes in disease. In the first place, the extreme rapidity with which all its changes occur, the consequent transientness of the phenomena, and the minute quantities in which several of the ingredients exist, oppose great obstacles to the research; but still greater embarrassment is caused by the extreme complication of the fluid. By "complication," I do not mean merely that it contains a large number of ingredients; but that those ingredients correspond to different dates of time, to different degrees of development, to different organs of formation. Mentally we can see with perfect distinctness, that in every porringer of blood drawn by the phlebotomist there do in reality co-exist three forms of blood—viz., 1st, blood not yet ripe, but in course of development—perhaps I should rather call it matter in a transition-state from food to blood; 2dly, blood which is already perfect, and which, at the moment of its abstraction, was actually doing the work of the economy; 3dly, blood which had done its work and was worn out; or, to speak more exactly, the waste material of those various organs and tissues which the blood had previously nourished. *Mentally*, I say, we can separate these three kinds of blood, but experimentally we cannot. They are mixed together—past, present, and future, (the blood of yesterday, the blood of to-day, and the blood of to-morrow,) and we have no method of separating them.

In all probability, the fibrin and extractive matters represent the waste products of the active elements of the body, and exist in the blood as effete material in the way to be eliminated; representing what just now, by a figure of speech, I called the blood of yesterday. Of the fibrin, I shall have plenty to say presently, and shall then explain to you why I consider it as an effete product in the blood. Of the extractive matters I know too little for me to dare to say much; hardly an endeavour has yet been made by any competent physiological chemist to refer them to the several organs in which they probably originate. Dr. Franz Simon, who has done with them more than any other chemist, divides them according to their respective menstrua into water-extract, alcohol-extract, proof-spirit-extract; but (as I need hardly suggest to you) that is not the sort of division likely to be useful to us in our present subject: the only physiological division would be one referring them severally to the organs whose effete products they represent: showing such an one to be brain-extract, another muscle-extract, &c. &c.

It is desirable, gentlemen, so far as may be possible in treating of blood-diseases, to contemplate them in the manner suggested in the physiological retrospect I have made, and to take them in some such order as the following: First, diseases depending on morbid ingestion; secondly, diseases depending on increase, arrest, or alteration of the excretions; thirdly, diseases depending on modification of the blood's own growth and development.

I. *Morbid Ingestion.*—This is, in fact, known to you under the other name of *poisoning*. But when we have a patient suddenly

dying or presenting symptoms under the effects of an active drug, we are sometimes apt to forget how important a part the blood plays in the production of phenomena. The symptoms of blood-disease are, in fact, generally quite lost in those of some secondary local affection. Where alcohol has been taken, the remarkable cerebral phenomena induce one to say that "it has got into the patient's head;"—and so it has; but its presence there has been preceded by its solution in the blood; and if a quantity of blood should be withdrawn at the time when alcoholic excitement is at its height, the process of distillation would conclusively attest the presence of the agent in question. You are, I dare say, aware of Magendie's celebrated experiments with poisons, particularly of those which he undertook to illustrate the transference of poisons by the blood. There are certain strong poisons, such as the wourali, which very rapidly diffuse their action over the entire system if a small portion be inserted into a recent wound. A little wourali thus inserted into an incision in a dog's foot would very rapidly prove fatal, under all ordinary circumstances; but Magendie found that if he previously tied the femoral vein, so as to prevent the general system of the circulation being contaminated by the poison, the symptoms were almost indefinitely postponed; he found, however, that directly he loosened his ligature on the vein, the poison (having passed on into the circulation) began to operate, and soon produced its characteristic fatal results. He invented, too, an ingenious way of demonstrating this still more strikingly; he would amputate a dog's leg, all but the artery and vein, so that the vessels should be the only medium of connection; or, more than this, he would divide these vessels, and join their upper to their lower sections by bits of quill or of catheter, still letting the blood flow on through the severed limb by means of these artificial pipes; and, not the less, did the symptoms of poison arise when there was no continuity of living tissue, no communication whatever except the flowing contaminated blood.

The same is true in respect of cases of slower operation: in a peasant, who has been eating diseased rye-bread for some weeks, and who presently, in consequence, has dry-gangrene of the extremities; or in a painter, who for months or years has been exposed to the poisonous contact of lead, and who has got paralysis of the extensor muscles of the wrist, with perhaps other nervous injury beside; or in a gilder, who has been for a similarly long period, inhaling the vapours of mercury, and is palsied in consequence;—in any such case, I say, you must not forget that the disease of the blood is the first link in the chain of cause and effect, and that the local affection, the excitement of brain, or the paralysis of muscles, or the obliteration of blood-vessels in the cases I have cited, or indeed any other morbid affection of a tissue or organ under similar circumstances, depends on that tissue or organ being nourished by a previously contaminated blood. If you take into the stomach a little rhubarb or iodide of potassium, and find traces of the drug in a few minutes in the urine, you know that, before arriving at the kidney, this material must have traversed the circulation; that it must have been absorbed

from the intestinal canal, have been dissolved in the serum, and literally have formed part of the blood during the time that elapsed between its absorption and its discharge. You see that this is pretty nearly the same thing as occurs in the natural processes of organic conversion. The urea, which the kidney naturally secretes, has not been developed in that organ, but has been formed at a distance from it—has been formed, in all probability, as a part of the series of chemical changes which occur in the active tissues of the body during the performance of their functions; then, in order to reach the kidney, has formed part of the stream of circulating blood, dissolved in its serum, and detectable there by chemical procedure.

While on this subject, too, I may take the opportunity of mentioning,—though I shall again have occasion to recur to it,—that the organs which display these secondary affections under the influence of poisons in the blood will always have appropriated a certain proportion of the poison into their substance, and will generally display it under chemical treatment, even more strikingly than the blood itself. Thus, for instance, in the post-mortem examination of a paralytic looking-glass silverer, you may have the certainty of discovering traces of mercury in the substance of the nervous centres, &c.

Now, to the affection of the blood by morbid ingesta, there are limitations set by nature which it may be well to consider. 1. A variety of poisons which would prove instantaneously fatal if they could enter the blood, are precluded from entering it—at all events rapidly. The mineral acids, for instance, would at once coagulate the albumen and destroy the fluidity of the blood; but this act is impossible in reality; for their first chemical action being exerted on the tissue with which they come into primary contact, they begin by disorganizing this, coagulating all the albumen in its capillaries, arresting its circulation, and thus opposing an effectual barrier to their own direct action on the blood of the general circulation. I think it little less than certain, though I have not the means of demonstrating it to you, that the action of corrosive sublimate is very importantly limited and retarded by this process; and I may suggest it, as a very proper subject for inquiry, whether the pneumonia which so often follows the action of corrosive poisons, may not, in some instances, depend on a mechanical stasis, or interference with the capillary circulation in the lungs, by means of coagulated albumen, which has been conveyed in the blood from the seat of the primary lesion, and has become arrested in the next ensuing minute vessels to which the circulation had hurried them.

There is another limit to the possibility of the blood's being poisoned, and this one acts almost or quite universally. I allude to the extreme rapidity of excretion, and I may inform you that this faculty, which forms an all-important provision for the safety and integrity of the blood, constitutes likewise (as you may conceive) a main source of difficulty in all chemical endeavours to demonstrate the passage of drugs and poisons through the circulation. I have already stated to you (and you may easily illustrate it for yourselves), that the elimination of a matter by one organ or surface of the body

is sometimes quite as rapid as its absorption by another. We are unable to decide what effect might be produced by the presence of a drachm of iodide of potassium in the blood, because, as soon as a few grains are absorbed from the stomach, the kidney and various mucous membranes begin to secrete fluids, which are impregnated with the drug, and which rapidly remove every trace of it from the circulation. Prussiate of potash has been detected in the urine two minutes after its introduction into the stomach. I can give you a striking instance of the completeness with which these transferences are effected without disorganization of the blood. An ounce of lactic acid was injected into the pleura of a dog, daily, for several days; twenty-four hours after the last injection, not only had the blood its normal reaction, but the serous effusion in the pleural cavity was likewise alkaline.

I must not leave the subject of morbid ingestion without two other allusions. In the first place, let me remind you of the ingestion of the so-called *morbid poisons*—the materials of infection in the specific communicable diseases. As I shall devote a lecture to the separate consideration of these influences, I may content myself now with indicating to you the point of contact between that subject and our present one, and with telling you, that undoubtedly it is by absorption into the blood, and by ulterior changes produced in that fluid, that the virus of scarlatina, of hydrophobia, of typhus, of syphilis, &c., obtain their power of infecting and injuring the whole economy.

Secondly, let me advert to the abnormal passage into the circulation of materials not having the fluid form—materials which act primarily as foreign bodies within the blood-vessels. I have already glanced at the possibility of coagulated albumen being transferred from one part of the circulating system to another, and presently forming plugs, and giving rise to congestions of blood in the part to which it has been conveyed. Starch, sawdust, and mercury, injected for the sake of experiment into the systemic veins of the lower animals, speedily get their particles impacted in the capillaries of the lung, and produce pneumonia there. This inflammation is often not very intense, and is circumscribed to the immediate vicinity of the foreign irritant or obstruent; after such an experiment, you will find a globule of mercury, or a few granules of silica, forming the centre of a little circle of inflammatory condensation in the lung, or perhaps of a little abscess, which, if left to itself, would presently have burst into any neighbouring bronchus, and would then have healed.

Sometimes the foreign materials thus introduced into the circulation are things having life, and susceptible of ulterior changes of their own; such as the growing germs of pus and cancer. In the practice of surgery, we very frequently have the opportunity of witnessing the effects of their presence in the blood, and the manner in which that presence is occasioned. In the progress of cancerous tumours, veins get laid open, often in such a manner that a portion of the morbid growth blocks the ulcerated opening of the vein, suffers the circulation for a while to pass on uninterruptedly, and from time to time sheds a batch of cells into the blood which washes over its

surface. Suppose this to be a systemic vein, and you will know that presently this blood, with cancer-germs suspended in it, must reach the right side of the heart, and thence be transmitted to the lungs: there—in capillaries which are adapted only for the corpuscles of the blood, the larger foreign cells are at once arrested as on a filter, and become the nucleus of secondary cancerous growths. Similarly with pus, suppuration may have occurred in some tissue which (like the cancellated structure of bone) abounds with large veins, and some of these may have ulcerated and have given entrance to the pus-cells; or in another case the vein may itself have been the seat of suppurative inflammation, and have suffered the products of this process to make way through the lining membrane into the blood; or (as very frequently happens in surgical operations) large veins may have been freely opened in immediate connection with surfaces likely to undergo acute suppuration; or (as I have seen in two instances) a small abscess in the muscular substance of the heart may discharge itself into the auricle or ventricle; or finally (as I have lately had occasion to witness), there may be the passage of pus from diseased lymphatics into the thoracic duct, and thence into the subclavian vein; and then, whether the admission of pus into the stream of blood have arisen in one way or the other, the results are uniform; the pus-cells are larger than the blood-corpuscles; they consequently become fixed in the smaller capillaries at which they next arrive, and give origin to what are called secondary abscesses.

It will be obvious to you that these secondary formations of pus and cancer (for both follow the same law) will be apt to occur *in the lungs*, when the primary disease has been in connection with some systemic vein; and that, on the contrary, they will present themselves *in the liver*, when some vein of the chylopoietic system has been the channel of infection. When secondary deposits have occurred in the lung, there is liability to the formation of innumerable tertiary deposits in other parts of the body: and, in regard of pus, this liability is extreme. I cannot tell you with certainty whether these ulterior formations depend on the diseased lung furnishing materials *de novo* for the contamination of the system; or whether, on the contrary, they arise from some of the original inflammatory products having (from their smaller size) escaped detention in the capillaries of the lung, and having subsequently (perhaps meanwhile grown larger) got entangled in the capillaries of the systemic circulation. The latter supposition is, on the whole, most accordant with the facts of the case; but I may tell you that it has never happened to me to see these scattered abscesses in the course of the aortic circulation, except where the lung itself has likewise been in a state of suppuration.

There is, you see, a very striking difference between the effects observed when these living things, these germs of pus and cancer, get into the circulating blood, and the derangements which arise (at first mechanical, and afterwards, to a very limited extent, inflammatory) when inorganic foreign bodies have found their way into the stream. The essential difference lies in the immense reproduction which fol-

lows the intra-vascular stasis of the former class of bodies. In the present state of our knowledge, it is impossible to decide with confidence as to the manner in which this occurs; but there are good reasons for believing that the transplanted germs (like the founders of a colony) become, in their new site, the agents of this multiplication. There are no sure grounds for determining whether the process occur at their expense; whether it consists in an actual development out of them; whether (by endogenous generation, or by some analogous method of breeding) the transplanted cells of pus or cancer stand in a *parental* relation to the secondary deposits which they occasion.

II. Having thus touched on the most important sources for contamination of the blood by ingestion of abnormal products, I now proceed to enumerate, under our second head, those diseased conditions of the blood which arise *in errors of egestion or excretion.*

1. Foremost among such morbid conditions we may consider, as a class, the *retention and accumulation* in the blood of matters which ought to be excreted.

a. Of all excretions, that of carbonic acid seems the most essential to the continuance of life, and any sudden interruption to its progress proves, as you know, immediately fatal. In warm-blooded animals, where the waste of tissue is incomparably more rapid than in the lower vertebrata, constant renewal of oxygen is indispensable to the function of the nervous centres, and privation of this gas proves *per se* a rapid cause of death; but in cold-blooded animals (where the need for oxygen is less urgent) we are able to observe, experimentally that asphyxia results not so much from the absence of oxygen as from the accumulation of carbonic acid in the blood, and that such animals live (comparatively speaking) a long time, if placed in an atmosphere of nitrogen or hydrogen gas, which, though destitute of oxygen, enables them, according to the well-known laws for the diffusion of gases, to eliminate their carbonic acid as fast as it is formed. We have many opportunities of recognizing the influence of carbonic acid on animal life as that of a poison, positively; and we can trace all degrees of this agency from that minor amount of inconvenience and injury sustained as we breathe an ill-ventilated atmosphere (that of an ordinary ball-room, for instance, or of the theatre at the College of Surgeons), up to the dramatic French suicides effected by the vapours of burning charcoal, or the rapid extinction of life in animals forced to respire the exhalations of the soil in the celebrated Grotta del Cane, near Naples. The state of blood brought about by any of these means is one in which the distinction of venous and arterial is more or less completely lost; the blood tends to become uniformly venous in its qualities; that is to say (whether taken from artery or vein), it has a dark colour, and an impaired coagulability.

Defective exhalation of carbonic acid attends a great variety of diseases in the human subject;—all, namely, in which the extent of respiratory surface is diminished by any organic disease of lung, or by a straitened capacity of chest; or in which the access of fresh air

is hindered by an obstruction of the larger air-tubes, or by a paralysis of the inspiratory muscles; or in which the heart is unable to maintain an active circulation through the lungs, so as to expose all parts of the blood with sufficient frequency to the influence of the atmosphere.

Chronic venosity of the blood (as it occurs in dependence on congenital malformations of the heart) is called *cyanosis;* and the blueness of surface from which this class of cases derives its name, depends on the insufficient exhalation of carbonic acid. The heart (owing to its mechanical imperfections) cannot circulate the blood rapidly enough, cannot expose it often enough to the action of the air; thus the carbonic acid accumulates, and maintains the blood in a venous condition; while, at the same time, the malformed organ, by delaying the systemic circulation and causing great congestion of the carbonated blood in the general capillary system, renders the unhealthy tint of the blood more apparent to the eye than it would be in any simple case of poisoning by carbonic acid. If the subjects of such diseases delay to die (as sometimes they do for years) they vegetate with a general torpor and feebleness of vitality, with an incapacity for muscular or even mental exertion, with an extreme susceptibility of fatigue, and with a defective resistance to cold, which sufficiently mark the morbid chemistry of their blood.

There is one signal peculiarity which attends this chronic venous condition of the blood, and which I must not leave unmentioned. Not only in extreme cases of cyanosis, but in all chronic diseases where, from any cause whatever, there is defective arterialization of the blood, the patient enjoys one privilege. He is exempt (perhaps absolutely, but at least, *all but absolutely* exempt) from tubercular diseases. And as the circumstances which interfere with due aëration of the blood are of the most various kinds (some of them acting merely mechanically), so we are justified in inferring, from the exemption just specified, that the condition of system in which tubercle is deposited is incompatible with venosity of the blood.

b. You are familiar with another illustration of retained excretion in the blood, as constituting the disease of *jaundice:* the phenomena of which depend, first, on the saturation of the liquor sanguinis by the colouring matter of the bile, subsequently on the deposition of this colouring matter in various tissues, and its admixture with various secretions. In the urine, especially, you see a large quantity carried off. As soon as the mechanical impediment to the flow of bile has been removed, and the secretion again takes its natural course into the duodenum, the urine rapidly recovers its natural hue, and so likewise, we may presume, does the serum of the blood. The skin is more permanently dyed, and recovers itself slowly: probably the colouring material is deposited there in a solid and scantily-soluble form. Vogel has noticed, in the tissues of persons who have died with jaundice, the presence of coarse granular deposits of an intensely yellow-red colour. In such cases, too, you may expect to find the colouring matter deposited in the nucleated cells of the glands which have been excreting it: in those of the kidney, for example, I have

often observed it. Of the real condition and changes of the blood in jaundice we know very little. We can in most instances account for the occurrence of the disease, either by finding evidence of a mechanical impediment to the passage of the secretion; or by having reason to believe that the secretion has been formed in sudden temporary excess, so as to flood the ducts and lobules of the liver: and in either of these cases we can understand the blood being tainted with bile. And we easily, with the eye, trace the apparent diffusion of the retained product in all parts to which the blood has access; but this is only as regards the colouring matter, for in respect of the essential constituent (bilin) we have little certain information. Sometimes this ingredient has been discovered in the urine by means of Pettenkofer's test, but by no means invariably; and yet it does not seem to accumulate in the blood. The subject derives great additional interest from the insignificance of the symptoms which often attend jaundice, and which we can scarcely suppose consistent with the suppression of so large an excretion. Whether the bilin may undergo decomposition in the blood, and may thus be brought within the excreting power of other organs, is a point as yet quite undecided, and on which accurate knowledge is very much required.

c. The most important disease under our present head is that deadly contamination, which the blood is liable to derive from the retention of *urea*, whenever the kidneys have become incapable of discharging that product from the system. It is thus that patients die with acute suppression of urine, or with the chronic effects of Bright's disease, poisoned by their own urea. The blood, loaded with this material, acts on the brain as a narcotic, and terminates life by coma and convulsions. Very often (especially where its accumulation in the blood is gradual, as in slow cases of kidney degeneration) the urea will act as an irritant of various tissues, especially of the serous membranes; the patients will be carried off by pleurisy or peritonitis, or sometimes by pneumonia. Many fatal attacks of inflammation, which at first might appear idiopathic, prove, on more careful inquiry, to be secondary effects of the state under consideration. In all cases where a large inflammatory effusion has occurred under the influence of an urinous contamination of the blood, you can demonstrate, by proper chemical tests, the presence of urea in that effusion, and can thus connect the fatal disease with the true cause of death. The vomiting and diarrhœa, which so frequently occur in connection with Bright's disease, have the same pathological origin: they consist in an irritation of the gastro-intestinal mucous membrane, by the morbid blood, and their tendency is to work off the poison by that secreting surface: a point to which I shall hereafter have occasion to recur.

2. A second, and a very important class of errors relative to egestion from the blood, is the opposite to that just spoken of—a class of diseases, namely, in which the blood is deranged by the occurrence of certain new, artificial, or otherwise abnormal excretions. Now these morbid drains from the system modify the blood chiefly in respect of its proportion of solid to fluid ingredients: they affect its

dilution, making it more or less watery than it should be; and, in doing this, they alter its specific gravity.

a. Inspissation of the blood, under such circumstances, is rare. You might at first think it would occur in diabetes, where the flux of water is so great; but when you remember the high specific gravity of the urine, and the vast quantity of solid matter running to waste in that excretion, you will be prepared to believe the contrary. And such is the case: the solids of the blood are relatively diminished in diabetes. Nothing can illustrate the waste of the economy in that disease, and the extreme degree in which nourishment is derived from its due course, more clearly than the fact that, despite the immense elimination of water, the specific gravity of the blood is below its standard.

The only disease (so far as I know) in which the excretions gain on the fluidity of the blood, so as to inspissate it, is cholera. Lecanu made several experiments upon the constitution of the blood in this disease, and found the water always materially reduced, in one case even to less than half the total weight of the blood examined. The following are his numbers:—

	Case 1.	Case 2.	Case 3.	Case 4.
Solid constituents . . .	251	330	340	520
Water	749	670	660	480

and in a separate analysis of the serum in cholera, which O'Shaughnessy published, the solid ingredients are given as more than 17 per cent. of the serum, instead of being 9 or 10 per cent.

This inspissation of the blood in cholera has, no doubt, much to do with the production of symptoms: the dulness and flaccidity of the cornea, the shrinking of the extremities, the imperfect aëration of the blood, and especially the stagnation of the blood-corpuscles in the Malpighian capillaries of the kidney, with the consequent suppression of urine, would all be probable physical results of so important a change in the fluidity and circulability of the blood. As regards the origin of that change in the blood, I need hardly tell you that the excretions, which pour by pailfuls from the intestinal canal with a rapidity unparalleled in disease, furnish a sufficient explanation.

b. Attenuation of the blood marks all other diseases which are attended by exhaustive discharges, and is their almost immediate result.

First among these may be counted hemorrhage. Ten of Cruveilhier's patients were bled three times. The mean condition of their blood, after each bleeding, was as follows:—

	At 1st bleeding.	At 2d bleeding.	At 3d bleeding.
Density of defibrinated blood . .	1056	1053	1049
Quantity of water in 1000 parts .	793	807.7	833.1
Solid residue	207	192.3	176.9
Corpuscles	129.2	116.3	99.2
Albumen	65	63.7	64.6
Fibrin	3.5	3.8	3.4

And MM. Becquerel and Rodier, who give these particulars, state that the effect of bleeding in impoverishing the blood increases with every venesection. This is likewise well illustrated in many of the tables which accompany the work of MM. Andral and Gavarret.* In their striking array of facts you will observe that the attenuation of the blood occurs almost exclusively at the expense of the corpuscles, the other constituents of the blood undergoing little change, in their proportion either to each other or to the entire mass. This law prevails in respect of all hemorrhagic affections, and of some exhaustive diseases besides. The albumen, for instance, you will observe, remains stationary, or nearly so. The physiological explanation of this fact appears to be as follows: After the abstraction of a considerable mass of blood, the volume of the circulation is restored by an increased absorption through the veins; the materials absorbed consist of those which had previously been exhaled from the capillaries into the interstices of the several organs, and into the

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* *Proportion of the several Ingredients of the Blood in Cases of Rheumatic Fever, illustrating the Changes effected by bleeding.*

Cases.	Bleedings.	Period of Disease.	Fibrin.	Globules.	Solid residue of the Serum. Organic.	Solid residue of the Serum. Inorganic.	Water.
No. 1	1	Day 3	4.9	101.3	78.4	8.1	807.3
	2	" 5	6.6	95.5	78.1	7.9	811.9
	3	" 7	6.5	85.2	90.5	7.8	810.0
	4	" 15	5.0	68.1	96.6	6.2	824.1
No. 2	1	" 4	8.9	109.3	84.7		797.1
	2	" 5	9.8	107.5	85.8		796.9
	3	" 6	8.5	95.4	83.6		812.5
	4	" 10	6.4	93.5	79.5		820.6
	5	" 25	2.8	117.9	89.6		789.7
No. 3	1	" 4	6.2	111.9	86.9		795.0
	2	" 19	3.7	102.0	82.8		801.5
	3	" 24	5.5	95 7	83.9		814.9
	4	" 34	5.8	81.5	78.9		833.8
No. 4	1	" 4	6.5	114.8	82.7		796.0
	2	" 5	6.2	111.0	82.1		800.7
	3	" 7	7.0	102.8	76.9		813.3
	4	" 10	6.9	88.7	80.5		823.9
	5	" 13	6.5	88.0	79.9		825.6
	6	" 15	6.8	76.6	79.1		837.5
No. 5	1	" 6	6.3	130.0	85.7	6.4	771.6
	2	" 7	8 2	112.5	80.8	6.8	791.7
	3	" 10	7.7	106.5	78.0	7.7	800.1
No. 6	1	" 7	9.3	103.4	79 0	7.5	800.8
No. 7	1	" 8	5 4	125 3	80.7	7.2	781.4
	2	" 9	7.0	124 9	78.7	7.1	782.3
	3	" 10	6.1	121.4	78.9	6.8	786.8
	4	" 14	5.4	99.6	76.0	6.1	812.9
	5	" 21	4.1	88.2	73.3	6.0	828 4
No. 8	1	" 8	6.1	123.1	84.2	7.8	778.8
	2	" 9	7.2	120.7	91.2		780.9
	3	" 10	7.8	112.8	91.4		788.0
	4	" 13	10.2	101.0	81.8	8.0	799.0
	5	" 17	9.0	89.2	81.4	6.5	813.9
	6	" 28	7.0	83.8	77.3	5.7	826.2

areolar tissue of the body, a fluid so nearly identical with serum, (differing only in its concentration,) that this constituent of the blood is soon replaced; but as the corpuscles can only be regenerated by a slower process of growth, each bleeding appears to have been made especially at their expense.

But still there are certain drains or excretions from the system which occur chiefly at the expense of the serum of the blood, and by which the albumen is consequently much reduced in its proportions. Protracted and extensive suppuration, or the discharge from large cancerous sores, or continued serous evacuations from the bowels, would act directly in diminishing the albuminous contents of the blood, as well as indirectly interfere with the regeneration of its corpuscles. In Bright's disease, where so much serum passes off with the urine, the same effect is observed ; in three cases, where Andral analyzed the blood, he found that the organic matters of the serum had fallen from their normal proportion (72 in 1000) to 61.5, 60.8, and 57.9 respectively. The development of hydatids in the liver (as it occurs in the rot of sheep) is attended by a similar result as regards the albumen ; and Andral, who first drew attention to the fact, states that sheep are liable to two distinct forms of anæmia, contrasted with each other in this particular : in the one form (analogous to chlorosis of the human subject) the corpuscles alone are diminished ; in the other (that which depends on the parasitic growth) the albumen, equally with the corpuscles, undergoes a marked diminution.

The attenuated condition of the blood, arising under any of these circumstances, produces an important secondary effect which is worthy of notice. You know that naturally the limitary membrane of the capillaries is a transudable tissue ; that it lets a certain quantity of the liquor sanguinis sweat through it ; and no doubt there is a definite proportion observed by nature in the construction of the body (according to its various local necessities), between the fluidity of the blood and the thickness and transudability of that limitary membrane, in the several organs where it is distributed. Now, in excessive attenuation of the blood, this proportion is destroyed ; the fluid is too penetrating for the tissue, and in consequence the membrane becomes too easily transuded by its contents. Such is the origin of those effusions into the areolar tissue (œdema) and into serous cavities, which are apt to occur when the serum of the blood is much de-albuminized. They do not arise in cases (of hemorrhage, for instance, or of chlorosis) where merely the corpuscles of the blood are relatively diminished ; but only when the liquor sanguinis has undergone some considerable reduction of density by the loss of its dissolved albumen. Their origin is purely physical : the animal membrane, under the same amount of pressure, suffering the partial transudation of its fluid contents with greater facility in proportion to the limpidity and low specific gravity of those contents. Of the composition of the fluids exhaled under these circumstances I shall have other opportunities of speaking.

LECTURE III.

Blood in disease, (continued.)—Cell-growth in blood; augmented in plethora; in menstruation; diminished in chlorosis. Therapeutic effects of iron explicable on general principles. Effects of spleen disease on the development of the blood. Serum; relation of its salts to production of scorbutus; (?) relation of its albumen to scrofulous and gouty deposits.(?) Extractive matters deferred to last lecture. Fat; conditions leading to piarhæmia. Fibrin; its signification in health, and that of hyperinosis in disease; fibrinous concretions in internal organs. Pathology of endocardial deposits.

Gentlemen: Having in my last lecture drawn your attention to those unhealthy states of the blood in which it has become contaminated from external sources, or overladen with effete matters that it cannot discharge, or starved and attenuated by some unnatural drain established at its expense;—having drawn your attention to these states in which the blood-disease appears secondary and incidental to some previous bodily disease, or to some obvious external lesion, I now proceed to consider those alterations which are referable to its growth and development, and which (comparatively speaking, at least) may be considered as primary diseases of the blood.

I. With respect to the Corpuscles. (1.) Their *proportionate increase* constitutes the condition of plethora: and probably, for the most part, this proportionate increase co-exists with an excess in the total quantity of circulating blood; so that not only are the vessels fuller than they ought to be—not only is the arterial pulse large, the venous stream full, and the capillary network throughout the body amply injected, but further, the blood which thus fills the vascular system is in itself of a richer and more intense quality than accords with perfect health. According to the analogy of other elements of the body, you might speak of this condition as hypertrophy of the blood. So little is known hitherto of the circumstances which determine it, that I cannot venture to say anything of its causes, except negatively. I may tell you, that although starvation will counteract the tendency to its occurrence, yet it cannot be referred exclusively to the quantities of food taken daily. Of many persons living together under similar circumstances, using precisely the same diet, and taking the same exercise, a certain proportion will tend towards plethora, while the remainder will retain a lower rate of blood-development; so that we can only leave it for the present as an ultimate fact, that—as the vital power in some persons tends to build large skeletons; in others, to accumulate fat; in others, to make bulky muscles; and this, in each case, without any assignable external cause but by virtue of some law relating to the diathesis of the individual, and inherent in him from birth;—so there are others who evince a similar liability to over-growth of the blood—to its formation, namely, in quantity or quality, out of proportion to the remaining development of the body.

Visceral congestions, especially of the brain and lungs, with a disposition to spontaneous hemorrhage, are the inconveniences which have been observed to accompany this condition of the blood, and any hemorrhage which may arise under such circumstances is to be considered critical and curative in its tendency. Most of you know, as a matter of familiar observation, how often the spontaneous occurrence of epistaxis or hemorrhoids will give complete temporary relief to the symptoms of plethora; and you will remember, from my last lecture, that nothing acts so efficiently as hemorrhage in producing that dilute and attenuated condition of the blood which is the diametrical opposite of plethora. Unfortunately, we cannot always with security leave this matter in Nature's hands; for she does not invariably select the capillaries of the rectum, or of the Schneiderian membrane, for the purpose of relief; sometimes, especially after the middle of life, when the arteries are becoming atheromatous and weak, the hemorrhage will take place in the brain, or in other important viscus, and endanger life.

The human female has a peculiar law of blood-development, which renders her a constant illustration of what I have stated to you. During about thirty years of her life she forms blood enough for herself and an infant. If she be pregnant or suckling, this redundant blood-formation fulfils its purpose of nourishing her own organism and what (as regards our present argument) may be considered the parasitic organism of her infant; but if she be neither pregnant nor suckling, then you will of course readily understand that the large blood-formation, which is normal to her for those necessities, becomes excessive in their absence,—thus exactly presenting the conditions I have spoken of as those of plethora; and, like other instances of plethora, this one tends to effect its own cure by means of recurrent hemorrhage—that, namely, from the mucous membrane of the uterus, which accompanies the discharge of unfertilized ova from the Graafian vesicles, and constitutes the periodical phenomenon of *menstruation*. Interruptions of this process most commonly occur from general causes affecting the blood-development, and keeping it below that abundance for which menstruation is the pre-ordained relief; and in these conditions of anæmia, whatever evils arise, are not caused by the suppression of the catamenia, but by that impoverished condition of blood which leads to their suppression: therefore such evils are the very opposite to those of plethora. But when, as occasionally happens, the blood-development is regular and ample, and the catamenia are suppressed merely because of some local disease, which renders the uterus incapable of its function, then all the general inconveniences of vascular fulness manifest themselves; and the plethora, which cannot vent itself by the legitimate channel, seeks a periodical relief at other surfaces, where it produces hæmatemesis, epistaxis, or hæmoptysis.

2. Far more frequent, however, than an increase in the proportion of the blood-corpuscles is that aberration from the standard of health which consists in their *proportionate decrease*. There is one disease which derives its visible characters from the non-development of the blood-corpuscles, and which consists essentially in that error;

and, after what I have just said on the pathology of menstruation, it cannot but interest you to know that the disease to which I allude (chlorosis) is eminently one of female puberty.

In fifteen cases of idiopathic anæmia, occurring in young women, Andral* found the proportion of blood-corpuscles varying, by successive degrees, from what he considers their normal standard (127) to so low a level as 30 in a thousand: and he found (precisely as would have occurred after large hemorrhages) that the water of the blood had increased just as the corpuscles had decreased, standing in one case as high as 886. In other particulars, he considered the blood healthy; but his estimate of fibrin for healthy blood is so liberal, that probably most computators would have differed from him in respect of these cases, and would have described them as presenting an excess of that material; and the organic residue of the serum is in most cases high. It is, however, quite evident, from examination of the various analyses which have been made, that the increase of fibrin (though often observed) is not essential to constitute chlorosis; that the disease substantially consists in an atrophic condition of the blood evinced in the non-development of its characteristic cells; and that the larger proportion of albumen generally found in connection with this state may fairly be explained, where it exists, as an acci-

* *Proportion of the various Constituents of the Blood in Fifteen Cases of Chlorosis.*—(From Andral & Gavarret.)

Cases.	Bleedings.	Fibrin.	Globules.	Solid Residue of Serum. Organic.	Solid Residue of Serum. Inorganic.	Water.
A. Commencing Chlorosis.						
First	1	5.3	99.7	84.2	7.2	803 6
	2	4.4	97.7	87.4	7.7	802.8
Second	1	2.5	104.7	91 0		801.8
Third	1	2.4	112.7	85.2		799.7
Fourth	1	3.6	112.2	83.1		801.1
	2	3.1	104 1	76.5		816.3
Fifth	1	3.3	113.7	87.4	5.6	790.0
	2	3.4	109.6	88.3	5.8	792.9
B. Confirmed Chlorosis.						
First	1	3.5	38.7	81.8	7.3	868.7
Second	1	3.0	46 6	83.9		866.5
	2	2.5	95.7	83.3		818.5
Third	1	3.5	49.7	94.0		852.8
	2	3.3	64 3	100.9		831.5
Fourth	1	2 8	49.6	87.5		860.1
Fifth	1	3.6	54.6	75.4		866.4
Sixth	1	2.6	56.9	80.2	8.7	851.6
Seventh	1	2.8	62.8	85.6		848 8
	2	2.1	49 0	81.0		867.9
Eighth	1	5.8	77.5	79.4	6.7	830.6
Ninth	1	7.4	70.1	77.0	5.9	839.6
Chlorosis in the Male.						
First	1	3 6	87.9	98 4		810.1
	2	3.4	77.2	87.9		831.5
	3	3.7	86.9	83.1	6.9	819.4

dental result of the defective cell-growth—which has left the serum more saturated with organic blastematous material than it could have remained if the normal proportion of blood-cells had been developed out of it.

Few of the effects of medicine are more immediate or more remarkable than that which results in this disease from the exhibition of iron. We all know, clinically, how soon under the influence of this remedy our patients recover their natural complexion; and a chemical analysis of the blood explains this sufficiently. F. Simon gives a case, where, after a few weeks of treatment, the proportion of blood-corpuscles rose from 32 to 95 in the thousand; Herberger, one where it rose from 38 to 98; Andral and Gavarret, one where it rose (in spite of two bleedings) from 46 to 95.

It is indeed very interesting to observe the effects of treatment tally so exactly with what is known of the pathology of this disease. As regards the influence of iron on the blood, we may with little hesitation describe it as a stimulant to the development of blood-cells; in which respect its action falls within a general law, (the evidence and bearings of which I shall have other opportunities of discussing with you,) that the specific stimulus of cell-growth, in every organ of the body indiscriminately, is a material identical with, or convertible into, the natural contents of the cell.

3. There is a third point relating to the morbid development of the blood-corpuscles, to which I must direct your attention, though I cannot, from my own knowledge, give you any very definite information about it. It appears that, in some diseased conditions of the spleen, the shaped elements of the blood become liable to change or to morbid admixture; sometimes large granular globules, two or three times as large as the natural-coloured corpuscles, have been found in abundance in the blood; sometimes the ordinary colourless corpuscles have been found in very great excess. The recent researches of Professor Koelliker (with which, no doubt, you have been made acquainted in the Physiological Lectures) render it highly probable that the blood-corpuscles naturally undergo their dissolution in the spleen, and that an early stage of this process consists in their being collected in groups within a cell-membrane, so as to form large granular globules, similar perhaps to those which, in certain cases of spleen-diseases, have been found within the stream of the general circulation; and although, since Koelliker's observations, no great progress has been made in the pathology of the spleen, yet what little has been noticed in regard of the blood, serves quite to establish the certainty that the spleen exercises some very important influence in its development; since this fluid, when observed in cases of spleen-disease, sometimes presents products apparently derived from that organ in an unfinished process of decay; sometimes, on the other hand, shows an extraordinary abundance of blood-corpuscles in an undeveloped, colourless condition. Within the last few days (through the kindness of Dr. Peacock) I have had the opportunity of examining a few drachms of blood from a child with enlarged spleen, now in the hospital, and it did not present any very obvious

deviation from the ordinary characters of blood; it coagulated perfectly, and brightened by exposure to the air; microscopical examination showed an abundance of colourless corpuscles, but not such an excess of them as to appear abnormal; and, among several specimens which I examined very carefully, I found only a solitary shape which I could suppose referrible to the spleen—viz., a faintly-marked cell, containing at one side of its cavity a cluster of three or four minute reddish-brown solid rods, such as are represented in Professor Koelliker's admirable article, (*Cyclopædia of Anatomy and Physiology*, Fig. 537,) and are considered by him to be final transformations of the colouring-matter of the blood. I noticed likewise a few such clusters without being able clearly to render visible any cell-membrane around them. In respect of the not extraordinary number of colourless corpuscles observed in this case, I ought to tell you that the patient had been submitted to the course of treatment which most of all tends to diminish the relative proportion of these corpuscles, by hastening their maturation into coloured blood-cells—namely, to the exhibition of iron.

II. As to the albumen and inorganic materials (salts and free alkali) which, with water, constitute the SERUM of the blood, there is just enough known to assure all philosophical observers that this is the most important branch of hæmatology; but as yet the materials are too unfinished for any extensive application. You know that the serum of lymph and blood constitutes the universal blastema, or atmosphere and material of growth, not only for the cell-development which incessantly advances within these fluids, but likewise for all other essential organic increase within the body. In my last lecture, I mentioned to you the physical consequences (leading to dropsical effusions) which arise from an attenuation of this fluid, when parasitic growths, or other albuminous drains, have removed its solid constituents in too great quantity; and I distinguished this attenuation of the serum, by the causes just mentioned, from that other partial impoverishment of the blood which depends on repeated hemorrhage, and which (being merely at the expense of its corpuscular contents) is, like chlorosis, unattended by dropsical effusions.

It has been thought that an increased saline impregnation of the serum might account for the phenomena of scorbutis; that it would give a physical tendency to cohesion of the corpuscles in the blood-vessels; that it would thus lead to local stasis of the blood in the capillaries, and, by rupture of these canals, to hemorrhage. Mr. Busk, the accomplished surgeon of the *Dreadnought*, published the analyses of three specimens of blood from persons suffering with sea-scurvy, in all of which the proportion of salts was much increased; namely, from 6.8 to 9.5, 10.9, and 11.5, respectively. But other analyses have been published, (particularly those of MM. Becquerel and Rodier,) from which it would appear, that the only certain and invariable character observed has been the advancing dilution of the blood, effected by a diminution not only of the globules, but of the solid constituents of the serum likewise. The inquiries which have

been made in this subject have been attended with the negative advantage of dispelling the old fiction, that the symptoms of scurvy depend on a solution of the corpuscles in the serum of the blood. Nothing of this sort is the case: scorbutic blood separates into clot and serum at least as readily as other blood; the serum remaining perfectly clear, and the clot (owing to an excess of fibrin) usually contracting with extreme firmness, and often presenting a buffy coat. In the present state of our knowledge, we are not familiar with any humoral change presented in scorbutus which can account mechanically and directly for the occurrence of those extravasations of blood which are characteristic of the disease; the state of the capillaries, however, forms a second element for inquiry in solving the pathology of that symptom; and it is at least worthy of consideration, whether the scorbutic blood-disease (supposing any such to be demonstrated) may not first act by affecting the nutrition, elasticity, and strength, of the limitary membrane of the capillary bloodvessels, so as to produce hemorrhage, not by the direct way of mechanical stasis and obstruction, but by the indirect way of weakening the capillaries and promoting their rupture.

Various diathetical diseases stand in a very intimate relation to the plasma of the blood, though at present it is not easy to refer them definitely to the albumen—much less to state the exact morbid process in which they originate. The humoral changes, for instance, which lead to the deposit of tubercle, may almost certainly be said to have their sphere of operation in the proteinous matters of the blood; and there are some grounds (to which I shall have occasion hereafter to refer) for suspecting that those changes especially relate to the constitution of its albumen. The phenomena of gout and rheumatism, again, obviously have their immediate origin in alterations of the blood; and there are reasons for believing that such alterations are primary, and constitute the essential nature of those diseases, respectively; but hitherto we are unable to hazard more than a conjecture as to the element especially altered, or as to the nature of the change. We know that, during the access of gout, lithic acid is generated abundantly in the blood by some intense and rapid process of chemical transformation; and the subsequent phenomena are those which attest the presence of such materials in the blood—namely, the occurrence of sudden local inflammations, and the appearance of the irritating material (lithic acid) among the inflammatory products. We know that, although lithic acid is normally an excretion of the body, yet gout cannot consist merely in the retention of that which ought to be eliminated; since, in cases of Bright's disease, lithic acid, no less than urea, has been found in the blood, without having produced symptoms at all resembling those of a paroxysm of gout. As to the source of the acid thus extensively formed—as to the element of the blood which undergoes transformation in order to furnish it, we have no certain knowledge; nor indeed have we more than a clue to inquiry for such knowledge, in the fact that any excessive addition to the albumen of the blood (especially under circumstances of low respiration) soon occasions an

inordinate excretion of lithate of ammonia by the kidneys, and thus inclines speculative persons to refer this excretion to that element of the blood.

III. Of the quantitative and qualitative changes to which the several so-called EXTRACTIVE MATTERS of the blood are liable, I am able to tell you nothing certain; but in a future lecture I shall have occasion to say something as to the pathological importance of these matters with respect to the doctrine of morbid poisons, and I defer any consideration of them to that opportunity.

IV. The FAT of the blood is subject to remarkable variations in quantity; and, whenever much augmented, it is liable to appear in a non-saponified state, in the form of free globules, which render the serum milky. The circumstances under which an over-fat condition of blood arises are so various, that it is difficult to make any statement of their nature which may apply equally to all cases. In some instances it is obvious that its excess depends only on the suppression of a secretion into which it ought to enter largely: in cases of jaundice, for example, the blood has repeatedly been found in this condition, and obviously has been overcharged with fatty materials, which the liver ought to have eliminated. Trail gives such a case, (one of hepatitis,) where the serum contained 45 per 1000 of oily matter. On a somewhat similar principle one may explain another concurrence which has been observed—that of milky serum with pneumonia and other acute diseases of the lung; since in these cases the oxidation of fatty materials in the blood is importantly hindered, and they are consequently allowed to accumulate. Similarly we may account for the occasional production of this state of blood in persons addicted to the intemperate use of alcohol; since in them the circulation is habitually loaded with artificial ingredients, which require oxygen for their elimination, and which therefore tend to supplant the natural excretion of hydro-carbon: in such cases the fatty contents of the blood will rise to 50 and upwards. During temporary gastric derangements, arising, in these persons, from aggravated indiscretions of diet, the amount of fat has been found very high: Lecanu analyzed the blood in such a case, (complicated by hæmatemesis, and therefore, perhaps, by disease of the liver,) and found fatty matters amounting to 117 in 1000. There are other instances, however, for which no explanation is easy. In diabetes the blood has been found fatty, and it may be doubted how far the loading of the blood by sugar would be sufficient to explain this on the principle just stated. Heller, too, gives a case of peritonitis, in which there was milky serum containing 50 per 1000 of fat: and I believe that many similar cases have been observed, where the blood has become fatty under the influence of inflammatory disease, even where the organ affected has apparently been quite disconnected from the function of excreting hydro-carbon. For such coincidences I am utterly unable to account.

V. The last ingredient of the blood, to the morbid variations of which I must refer, is in some respects the most important of the series: I mean, FIBRIN. I may take for granted that you are familiar with the general phenomena of coagulation of the blood; how the healthy blood, which runs so glibly in the pipes of the living body, and which spirts so fluently from a puncture in any one of them, is scarcely brought to rest in any receptacle out of the body before it begins to gelatinize, and within a few minutes sets into a uniform solid mass; that this gradually contracts and condenses itself, squeezing out from its interstices a perfectly clear albuminous fluid, and thus establishing the distinction between the *clot* and the *serum* of the blood. You know, likewise, that this distinction has no counterpart in the living blood as it flows in the vessels; but that the clot consists of the corpuscles entangled and bound together in the gelatinization of a material naturally distinct from them—a material which during life is dissolved in the serum, and with it constitutes the *liquor sanguinis* or plasma of the blood; so that the coagulum consists of the corpuscles *plus* the fibrin of the blood, while the serum consists of the plasma *minus* that same fibrin. According to the healthy rate of coagulation, (a rate which, though it immediately depends on the quality of the fibrin, is yet indirectly a pretty accurate measure of its quantity,) the gelatinized blood forms, as I have said, a uniform mass; a mass, too, which preserves its uniformity when it has contracted in bulk, and has discharged the serum from its interstices. But when the coagulation is retarded (as it is apt to be whenever the fibrin is in excess) the corpuscles begin to sink in the fluid before the latter is sufficiently gelatinous to fix them, and the clot becomes distinguished into an upper layer destitute of corpuscles, and a lower one containing them in excess. The upper layer, having its contraction less hindered by intervening material, condenses itself into much smaller compass than the lower; so that such a clot takes the shape of a truncated cone, the upper yellow stratum of which, somewhat turned in at its edges, consists of almost pure fibrin, and occasions the mass of blood to which it belongs to be called *cupped* and *buffy*.

One of the first points observed in the examination of the blood in disease was the frequency with which this appearance concurred with the existence of inflammatory affections; but on more extended inquiry it was found likewise to present itself in a variety of other conditions. To all of these conditions, however, there belongs the one common point of an absolute or disproportionate excess of fibrin.

Few points are more striking in the pathology of the blood than the constancy with which inflammatory diseases augment the fibrin: in acute rheumatism, in pneumonia, bronchitis, pleurisy, peritonitis, quinsy, erysipelas—this constituent has been observed increasing to the double, triple, quadruple, quintuple, of its normal amount. Pathologists, perhaps too hastily, were disposed to associate this increase with the constructive or organizing processes which com-

monly follow on inflammation, and to look on the augmented fibrin as tending to the final purpose of some additional growth.

This is a matter of great importance, and you cannot do justice to it without reflecting carefully on the natural functions of fibrin. Many physiologists have regarded fibrin as that ingredient of the blood which, in the ascending scale of development, stands next for appropriation into the living textures of the body: they have regarded it as representing the ripeness and perfection and nutritiveness of the blood. On the opposite side, of late years, have been some who incline to a very different view, thinking that they find cogent reasons for placing fibrin on the same scale as the extractive matters, and for reckoning it among those elements which have arisen in the blood from its own decay, or have reverted to it from the waste of the tissues.* I may confess that, to my mind, this appears infinitely the more plausible view, and I will tell you the arguments which induce me to adopt it.

First, I find that fibrin is undiminished by bleeding, however frequently repeated; nay, that it often, or even usually, increases under this debilitating treatment: its highest figure given in Andral's book (10.2) was at a fourth bleeding: and Scherer found it as high as 12.7 at the third venesection in a case of pneumonia. I find that under many other circumstances of exhaustion and weakness and inanition, during the progress of starvation,† during diseases essentially anæmic, during violent fatigue, and the like, its proportion has been found at least as high, perhaps higher, than in the inflammatory process. And as in these respects I find its proceeding to be in direct contrast to that of the red-globules (which we know to be potential elements in the blood, and which are at once reduced by bleeding or starvation) so also do I find a similar contrast in another striking particular. Messrs. Andral and Gavarret, in the course of their extensive researches in the comparative physiology of the blood, ascertained that an improvement in the breed of an animal tended always (*cæteris paribus*) to increase the proportion of its coloured blood-corpuscles; they found that the same improvement tended likewise to diminish the proportion of its fibrin. And I find further indications of the same inverse ratio between the fibrinousness and the perfection of the blood, in the facts—that there is little or no fibrin in the blood of the fœtus, none in the egg, none in the chyme, and less in the blood of the carnivora (who feed on it) than in that of the herbivora.

Some of these facts, derived from very different sources, appear quite inexplicable on the theory that fibrin is essential to the progressive development of the tissues; and the opposite inference seems

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* The latter view has been especially well argued by Dr. Zimmermann, in various writings published during the last six years.

† In analyzing the blood of seventeen healthy horses, Andral and Gavarret found the maximum of fibrin to be 5 per 1000; the minimum to be 3; the mean to be 4. In dealing with diseased horses, many of them meagre and half-starved, Dr. Franz Simon found this proportion increased to 11 or 12 per 1000. In one case, particularly, of experimental starvation of a horse, after four days' total abstinence, this observer found that the animal's proportion of fibrin had risen from 5 to 9.

unavoidable, that it must be considered an excrementitious product, derived from the waste of the tissues or the oxidation of the blood, and in progress of elimination from the system. This conclusion, carried into the domain of pathology, would lead us to suppose that an augmented proportion of fibrin in the blood (whether occurring in active disease, or within the limits of apparent health) can be taken as an indication only of increased labour and waste in certain elements of the body, not of an increased development in the resources and nutrition of the blood. And on the same grounds it would appear that a super-fibrination of the blood, in acute inflammatory diseases, must be regarded as a consequence and effect of those diseases, not as their cause, and not as a primary affection. Still, no doubt there are certain evils which result from the blood being thus overloaded with fibrin—evils to which that secondary affection has, in its turn, become a primary cause; and of these I proceed to speak.

What are called fibrinous concretions in the spleen, and kidney, and liver, have been ascribed by many authors to this humoral source.

It happens, somewhat frequently as respects the spleen, and not very rarely with the kidney, that in making post-mortem examinations we find a circumscribed portion of the organ remarkably dense, and firm, and bloodless, having a more or less yellow colour. These diseased portions have always an irregular outline, and are very abruptly defined; as abruptly as a clot of blood would be in the same place; but, unlike a clot, they are never red. When examined microscopically, they show no trace of true organization, no growth of new cells or of fibre; but they exhibit usually some increase in the normal elements of the organ, infiltrated with a large quantity of fibrin, which sometimes has considerable cohesion, sometimes inclines to be more or less molecular. I have never seen in these deposits any signs of progressive development, but it is frequent to see in them what must be considered evidence of a tendency to degenerate; for where the deposit is molecular, it always contains a considerable quantity of fat. In the specimen of spleen of which I show you a drawing, the proportion of fat was large, and the fibrin was undergoing that softening process into a product somewhat resembling pus, which Mr. Gulliver first and accurately described as often breaking up the substance of coagula in veins. I suspect that something similar occasionally befalls fibrinous deposits in the kidney. No doubt you have all seen many times those common cysts of the kidney which are so frequent in connection with Bright's disease, occurring of all sizes, from the microscopical upwards, and remarkable always (whether on the surface, or in the interior of the gland) by their globular shape and distinct membranous boundary. But occasionally, though rarely, there may be seen on the surface of the kidney another form of cyst, if cyst it can be called—a space, namely, just under the fibrous membrane of the kidney, (which in such cases has been adherent round it,) of irregular outline, much more extensive in superficies than in depth, having no lining membrane of its own, and containing only an abundance of greasy mat-

ter, partly as free oil, partly as cholesterine, partly as large cells, containing molecular oil globules. Now these false cysts have so exactly the shape which the fibrinous concretions affect, and their contents are so exactly like those which are found where fibrin has undergone degeneration, that I have been led to suspect a connection between the two, and to believe that they represent fibrinous concretions in a state of degeneration and decay.

As these peculiar concretions in internal organs are never recognized during life, and as we have no satisfactory means for measuring the fibrin of the blood after death, I cannot tell you how far the popular opinion is right which refers them to an over-fibrinous condition of the blood. In some instances which I have recently examined, I have found considerable disease in the arteries of the part; quite enough to account for the amount of local disease. Fibrinous concretions in the spleen, which are most frequent, very generally coincide with valvular disease of the heart.

The next evil which I have to speak of as a consequence, or probable consequence, of the over-fibrinous condition of the blood, is of the greatest interest. Those of you who have attended physicians' practice, and have watched cases of rheumatic fever, know with how much anxiety, from day to day, the stethoscope is applied to the patient's chest: not necessarily because he complains of pain there: his attention is confined probably to his swollen wrists and knees: but, while he is groaning about them, there may be mischief advancing within his chest—mischief readily indicated to the ear of the physician, but perhaps utterly unattended with pain to the patient; and which, notwithstanding its painlessness, is infinitely more serious than all the patient's articular agonies put together. I allude to those fibrinous concretions on the valves of the heart which have (as I think too hastily) been called results of inflammation—of *endocarditis;* and which no doubt often arise in persons of the rheumatic diathesis, without any violent and explosive attack of rheumatic fever.

As the question "How do these valve-diseases originate?" is one of the greatest practical importance (for it must materially influence the method of treatment), I shall enter at length upon the theory of their formation.

The general opinion, which till very lately has been unquestioned, is, that the lining membrane inflames, and pours out lymph (just as the pleura or pericardium might do), and that thus these vegetations are true *excrescences*, which have arisen in an inflammatory exudation.

Now here, on the threshold of the subject, a doubt occurs—Is the lining membrane of the arterial system susceptible of inflammation? "Inflammation," in the language of the schools, "consists in an increased action of the bloodvessels of a part." Without pledging ourselves for the accuracy of this definition, we may use it in the present instance as a rough criterion of inflammation; at least negatively. No part can be said to inflame, in the ordinary sense of the word, which has not vessels of its own. You cannot talk of

inflammation of the hair or nails. What, then, are the bloodvessels of the lining membrane of the arterial system, which this theory supposes to be the seat of an increased action? That portion of an artery which we term its inner coat has no bloodvessels of its own, nor do those of the middle or contractile coat (which are derived from the so-called *vasa vasorum*) penetrate to a sufficient depth to influence materially (if at all) the nutrition of the lining membrane.

In the Museum of the College of Surgeons there is a preparation of M. Quekett's (an injection done, as all Mr. Quekett's are, with admirable success), which shows how very much the *vasa vasorum* fall short of reaching the lining membrane of the artery. And—if you will but think for a moment, what should *vasa vasorum* do there? what could they convey more fit for the nutrition and growth of the membrane than what is already there?—than that blood, namely, which is already washing over it incessantly and profusely.

And again, gentlemen, reflect on this: the lining membrane of the artery and of the valves has an epithelium; wherever epithelium grows, the old cells drop off in a direction opposite to that whence the new ones derive their materials of growth. Just as our scales of epidermis drop from the surface of our bodies, being nourished and renewed from within; just so, if the epithelium of an artery were renewed from without (i. e. by *vasa vasorum*), the old scales, as fast as they became detached, would drop into the interior of the vessel; and though, no doubt, their decay is very slight, and the number that might thus pass into the circulation, and presently obstruct the capillaries, would be very small, still it would be essentially a clumsy arrangement.

From a variety of reasons, it seems almost certain that the ordinary nutrition of the lining membrane of the circulating system is derived directly from the blood with which it has contact; and that its morbid changes depend—not on any inflammatory condition due to the *vasa vasorum*, but on those humoral changes, those variations in the qualities of the blood, by which it is more immediately and more certainly affected than any tissne of the body.

On these grounds there would be great *primâ facie* difficulty in believing that the endocardial deposits could be of inflammatory origin. But this is not all; for, if they were inflammatory exudations, why should they be so peculiarly limited to projecting or uneven surfaces of the lining membrane? And why should they evince so decided a preference for the *left* side of the heart? Both sides of the heart, and all points of each cavity, are (one would think) equally exposed to the causes of inflammation; the coronary arteries supply both ventricles of the heart indifferently, and we well know that acute *peri*-carditis pays no respect to the grooves and septum of the heart; it traverses all such lines of demarkation, injects the bloodvessels of right and left side alike, and covers ventricles and auricles equally with its dense inflammatory exudation. On the supposition that these vegetations are inflammatory effusions from the membrane, I should be quite unable to explain why they

should almost entirely confine themselves, as they do, to the valvular apparatus; and why their predilection for the left side should be so great, that the right is very rarely affected—perhaps never, except where the left has first suffered, and where the disease has been of such extreme intensity, that even its weaker affinity for the right side has been able to manifest itself.

The opposite doctrine is the more tenable one. I believe that the origin of these vegetations is directly humoral; that they arise as fibrinous precipitations from an overcharged solution; the valves incrusting themselves with fibrin, just as a stick in certain streams coats itself with a calcareous envelope; and that the preference shown for the left side of the heart admits of explanation by reference to the peculiarities of its contents—the new-made arterial blood.

You will observe that this theory involves the supposition, that arterial blood is more prone than venous blood to precipitate its fibrin, either as containing more of it, or as containing it in some more separable form.

Not wishing to leave this a matter of uncertainty, I have experimented on the subject. I have carried a single thread, by means of a very fine needle, transversely through the artery and vein of a dog, leaving it there so that it might cut the stream; and I have done this repeatedly, sometimes in the femoral vessels, sometimes with the carotid and jugular, sometimes with the aorta and cava. I have suffered the thread to remain during a period of from twelve to twenty-four hours. My experiments have given me as a uniform result, that the arterial blood with the utmost readiness deposits its fibrin on the thread; the venous blood with the utmost reluctancy. And in most of my experiments, the thread, where it traversed the canal of the artery, presented a very considerable vegetation on its surface, (exactly like those we are talking of on the valves of the heart;) a vegetation sometimes as large as a grain of wheat; always of a pyramidal shape, with its apex down-stream, and its base attached to the thread. In the artery, one might say that the thread whipped the blood, just as one whips blood in a basin to get the fibrin out of it; but with this trifling difference, that, instead of the rod beating the fluid, the fluid ran over the rod and precipitated its fibrin there. In the vein, the thread seemed to operate no way but obstructively; never coating itself with fibrin, but sometimes delaying or stopping the circulation with a voluminous black clot, chiefly collected on that side of the thread remotest from the heart. Accordingly, the general statement and rationale of the matter appear to be as follows: the disease in which these deposits are so frequent is one of intense over-fibrination of the blood, and one in which almost certainly there are other conditions, besides *quantity*, making the fibrin easy of precipitation; the left side of the heart has preference, because it is the arterial side, and because arterial blood, as we have seen, readily parts with its fibrin; the valves, and particularly their streamward surfaces, are chosen for the deposit, because their position exposes them chiefly to the fric-

tion of the current; so that the whole curious selection of site for the deposit resolves itself into the concurrence of two conditions, which are fulfilled in that one spot of the vascular system—namely, the greatest chemical tendency to the deposition of fibrin, with the greatest mechanical facilities for its entanglement.

In introducing this subject, I mentioned that it is one of great practical importance. Many people bleed locally, or even generally, when they hear an endocardial murmur arising in the course of rheumatic fever. In their eyes, the new disease is endocarditis; and everything ending in *-itis* is thought, in at least a majority of instances, to be benefited by bleeding. Therefore, gentlemen, do not be in a hurry to call it endocarditis; and, as for bleeding, all that I would venture to say (for of course the treatment of this physician's disease does not fall within my province) is, to assure you of the pathological fact, that you may bleed a patient to death without altering (except probably to increase) the proportion of fibrin in his blood.

I may mention, however, as of some pathological interest, that in a recent work on Diseases of the Joints, by a French surgeon of considerable experience, (M. Bonnet of Lyons,) a section is devoted to the treatment of acute rheumatism by nitrate of potass in large doses, (up to an ounce or an ounce and a half per diem.) He speaks of its utility in the highest terms, and he quotes with full concurrence a passage from M. Gendrin, who has likewise used the medicine very extensively, to the remarkable effect that this method of treatment possesses this among other advantages, that it prevents inflammation of the endocardium—*il prévient les endocardites*. You will find an interesting paper, on the same method of treatment, communicated by Dr. Basham to the Medico-Chirurgical Society, and published in the last volume of their *Transactions*.

Now we know that nitrate of potash is a powerful solvent of fibrin; we know that in these large doses a quantity of it must be retained in the blood, and we are thus enabled to interpret the efficiency of the remedy in accordance with our knowledge of the disease. Nitre, if present in the blood in sufficient quantities, would prevent fibrinous concretions on the valves, by increasing the solubility of their material, and diminishing its liability to precipitation.

LECTURE IV.

Irregular distribution of blood; local hyperæmia. (a) PASSIVE: its mechanical causes; exudation; peculiarities of exuded fluid; instances of passive hyperæmia, and of its effects. (b) ACTIVE: Physiology of fluctuating supplies of blood; influence of nervous system over heart and arteries; muscularity of arteries; injuries of sensitive nerves affecting nutrition; neuropathic theory of inflammation.

GENTLEMEN: Having, in my last lectures, spoken of diseases which consist in *qualitative* derangements of the blood, and which relate either to the proportion of its natural ingredients, or to the introduction of new and poisonous material; I have now, in pursuance of my plan, to consider the subject of its irregular *quantitative* distribution.

The local supply of blood may be in excess, or in deficiency, of its right proportion.

HYPERÆMIA (literally over-bloodedness) is the most convenient word for expressing the former of the errors alluded to; and, as I need not remind you that the blood circulates—that it naturally passes in a continuous stream throughout all organs, and amidst all textures of the body, new blood being constantly brought by the arteries while the previous quantity is propelled into the veins,—so you will readily see, that the conditions of hyperæmia are twofold; viz., too much blood may be brought into a part, which constitutes *active* hyperæmia; or too little may pass out of a part in proportion to what flows into it, and this gives the state of *passive* hyperæmia.

The latter—the *passive* disease (often called congestion)—is the simpler for study, and I shall therefore begin with it.

Its conditions and consequences are purely mechanical. Tie or compress a vein for any length of time, and what are the results? The part whence the venous radicles arise become gorged with blood, which can no longer move on, to make room for fresh supplies arising from the heart; the part becomes larger and larger, more and more tense, and as it were fluctuating. I know of no organ which illustrates this condition better than the spleen, since its functions require that its veins should be eminently susceptible of passive distension; and where circumstances have interfered with a free flow of blood through the splenic vein, we find the spleen dilated, by passive hyperæmia, to an almost incredible size.

But, while the onward passage of blood is thus delayed, while the repletion of the capillaries goes on, and while that very delicate limitary membrane which forms their channel becomes more and more stretched with accumulating contents, a certain quantity of blood sweats through this very tense and very delicate membrane; or (to speak more correctly) the serum filters through, leaving the corpus-

cles still in the stream within. Now, I may remind you, that the sweating through of a certain quantity of *liquor sanguinis* is a healthy process: it is thus that the tissues are nourished; if the capillaries did not suffer this certain quantity to transude for feeding the parts to which they are distributed, then the circulation would be a fruitless performance; the blood might as well be in a bottle. You may say of all growing parts of the body that their elements lie in an atmosphere of fluid material derived by transudation from the capillary bloodvessels—material constantly renewed from the same source, and possessing all the characters of the original fluid, (*i.e.* of the *liquor sanguinis*,) with no other differences than those of a varying concentration.

The effect, then, to which I have to direct your attention as the first result of passive hyperæmia is, that this natural moisture becomes exaggerated; there is a larger than natural effusion into the interstices of organs, or into serous cavities—producing in the one case, œdema; in the other, encysted dropsy. The conditions of this process are probably, as I have told you, purely mechanical: increased exudation through the porous walls of a tube following increased hydrostatic pressure.

But there are one or two circumstances connected with the effusion which still require explanation. If you look at the table,* you will see that the fluid is sometimes very diluted, containing far less solid material than is dissolved in the serum of the blood. It usually contains no fibrin, or a mere trace of that ingredient; and its proportion of albumen is very low in comparison with that of the intra-vascular serum. How is this? If the fluid sweats through, does it leave its fibrin and part of its albumen behind it, within the vessels, or in their walls? The answer to this question probably must be affirmative; but the process is not, therefore, necessarily removed from the list of physical phenomena.

We know that the physical property of membranes, to imbibe and be permeated by fluids, is one which often combines with itself the power of effecting certain qualitative changes in the filtering fluid. If you fill a wet bladder with a mixture of alcohol and water, evaporation will go on from the surface of the bladder—evaporation, not of the whole mixture at first, but of water only; so that the contents get less and less watery. The wet bladder is more trans-

* *Analyses of Non-Inflammatory Serous Effusions.* (Vogel.)

Per 1000 parts of the Fluid.	Serum of Blood.	Hydrocele.	Hydrocele.	Ascites.	Ascites.	Ascites.	Ascites.
Water	905	920	927	946	956	988	704
Albumen	78	..	48	33	29	0.9	290
Extractive matters	4.2	71.5	10	13	..	..	2
Fat	3.8	..	9		7	10	
Salts	9	8.5	6	8	8		4
	1000	1000	1000	1000	1000	998.9	1000

udable by water than by spirit-and-water. And more to the point still is an experiment of Valentin's: having mixed water and albumen to a certain specific gravity, and placed the solution on a filter of stretched serous membrane, he found that the fluid, after traversing the filter, was of a reduced specific gravity; in other words, the fluid did not pass through in its original strength, but in a weaker form.*

Accordingly, though we are unable to explain the manner in which this change is effected, there seems no sufficient reason for removing it from the list of physical phenomena; and we may admit, as a general statement of the peculiarity of such effusions, that they vary in their original density according to the amount of pressure which determines their occurrence. But there is another element to be considered as helping to explain the difference between the *liquor sanguinis* and the fluid products of passive hyperæmia. Suppose, for a moment, that the former transudes without any diminution of its contents, and with all its original density;—it would then immediately become exposed to the action of the *lymphatics;* and their operation would no doubt suffice to alter its constitution, both rapidly and materially. Their action, too, would be just in the direction we are considering; for all the little we know of that action tells us, that they would withdraw from the effused material a considerable proportion of its animal ingredients. A glance at the table will show you that it is in this respect particularly, more than in regard of salts, that the products of passive hyperæmia differ from the plasma of blood; and those of you who have examined the large œdematous lower limbs occasionally seen in the dissecting-room, know how very visible, and how very full, in such cases, are the lymphatic vessels in the thigh.

But the effects of passive hyperæmia need not stop with the mere increase of exudation through the walls of the vessels; these may burst, giving rise to hemorrhage either in the interstices of organs, or on the free surface of mucous membranes. Such hemorrhage

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* There are two striking experiments to a somewhat similar effect, given by Matteucci in his Lectures on the Physical Phenomena of Living Beings: one of them is his own, the other is by Berzelius. If you fill a long tube with sand, and let a solution of common salt filter along it, the fluid which first escapes will be almost destitute of salt—will be almost pure water. Or if, instead of salt, carbonate of soda be used, the fluid which first escapes will be of greater density, and will contain a larger proportion of carbonate of soda than the original fluid. In most instances, however, of the latter class, where inorganic filters alter the fluids which traverse them, as to their density and proportions of admixture, there is a peculiarity distinguishing such cases from that which we are considering in the living body;—namely, the inorganic filter soon loses its power; its substance becomes saturated with whatever constitutes the difference between the filtrated and unfiltrated fluid; and beyond this point of saturation, it suffers the fluid to pass through unchanged. The only perpetual filters are those in which *growth* occurs, and where the growing organisms constantly appropriate that which is differential in the two fluids. A clay soil, for instance, furnishing the materials for vegetation, may, practically speaking, be a perpetual filter; all manner of impure fetid organic and saline solutions may be thrown on its surface; and nothing may run off in the sub-soil drains but a water almost as pure as if it had been distilled; its previous contents having remained on the filter, (just as in Matteucci's experiment with the sand,) but not saturating it, because of the vegetation which constantly withdraws them, and leaves the soil free for further action of the same sort.

can only occur by the rupture of vessels. When you look after death at the surface of a mucous membrane which has bled largely, or when you look (if you ever have the opportunity) at a uterus actually engaged in the process of menstruation, do not expect to see a large hole with blood spurting from it; that is by no means necessary. But holes there must be, whether seen by the naked eye or not. The notion of blood passing through the walls of a vessel, without any lesion of the latter, is one that could only belong to times when the structure of minute vessels was unknown. Mechanical laws apply to small things as well as to large ones. Capillaries naturally possess delicate, but perfectly solid and continuous walls; and it is just as impossible for a single blood-corpuscle to get through that wall without a hole being made for it, as it would be impossible for the entire man to sink through the floor of an apartment without an aperture of his own size existing for his passage. Microscopical examination quite confirms this view, by showing us an abundance of distended and broken capillaries in the structure of organs where hemorrhage has occurred.

In the ground we have gone over, simple as may have appeared many of the statements and explanations, lies the pathological knowledge of a great number of striking symptoms witnessed during life.

As respects chronic disease, at least, you find that the disposition of parts to become the seats of serous effusion and passive hemorrhage is in exact proportion to the liabilities they incur of having their return of blood interfered with, either from causes of their own, or in the progress of other disorders. Contrast, for instance, the lower with the upper extremities; or the mucous membrane of the rectum with that of the conjunctiva and frontal sinuses; and you see at once how effectually such influences operate. In medical practice you find abundant illustrations of the effects of passive hyperæmia. Take for instance the complications which arise in the progress of a case of chronic inflammation and contraction of the liver—cirrhosis, as it is called. You know that in such a case it is very frequent to find serous effusion into the cavity of the peritoneum, and hemorrhage from the mucous membrane of the stomach or intestines, giving rise to vomiting of blood, or to those black, bloody stools, which the physicians call *melæna.* Now all these secondary symptoms of the disease arise from passive hyperæmia; the contracted liver will not allow the blood freely to traverse it; consequently the vena portæ becomes gorged; then the splenic and gastric, and mesenteric veins which form the porta; then the capillaries, from which these veins arise in the serous and mucous membranes of the abdomen; and then occur increased exudation and hemorrhage. Or, take a case of defective mitral valve; at every beat of the heart a certain quantity of blood regurgitates towards the lung, and this organ becomes congested; you find the chest becoming less resonant than it should be, and you find your patient suffering with profuse serous expectoration, or evincing symptoms of pulmonary apoplexy.

Passive hyperæmia does not, I believe, in any degree conduce to the hypertrophy of parts. On the contrary, though the congested tissues contain far more than their normal share of blood, they are apt to fall into atrophy. Thus it is that ulcers of the lower extremity so commonly arise where the veins are varicose, and where the integuments are habitually the seat of passive hyperæmia. The rationale of this will be obvious to you on reflection. It is true that much blood is contained in the affected tissue; but it is blood that has insufficient means of renewing itself; and from its long detention in the part it acquires in an extreme degree the character of venous blood. Thus, as regards mere bulk of blood, the part is over supplied; but, in respect of the quality of blood, it may be said to suffer what is equivalent to anæmia: accordingly, the elements of its texture fall into a state of atrophic softening, which terminates in the formation of an ulcer. I think it not improbable that the same fact may contribute to explain the continued non-development of those effusions which arise from passive hyperæmia; and that these dropsies refuse to undergo the organic changes, which we shall hereafter find prevalent in the results of active hyperæmia—partly, perhaps, by reason of their greater dilution, but still more because the circumstances of stagnation under which they arise are such as, *ipso facto*, prohibit that change of material and renewal of nourishment which are indispensable conditions of growth.

II. From passive hyperæmia, with its mechanical causes and physical consequences, I pass to a topic of higher interest and greater difficulty—*active hyperæmia*—the going of more blood to a part than (except for the temporary circumstances of excitement) ought naturally to go there. This phrase includes that condition of blood-vessels which conduces to the inflammatory process, as well as that which enters into the process of hypertrophy; but I may tell you at starting, that it is not my intention, in the present lecture, to give any detailed account of those minuter changes which affect the circulation in inflamed parts. Mr. Green has taught you these in the Surgical Lectures; therefore I shall confine myself now to that general pathological argument which connects the inflammatory process with other variations in the nourishment of parts; and, in a later lecture, I shall have occasion to speak of some of the organized products of inflammation.

The physiological pre-condition of both hypertrophy and inflammation may be expressed in the following general formula, viz.: that there exists in the organism an arrangement for providing the elements of parts, according to their requirements, with an increased supply of developable blastema. The words "developable blastema" might seem at first hearing such as could readily give place to the word "blood." But the phrases are, for my purpose, not exactly equivalent; in the first place, because some tissues (the cornea, for instance, and many cartilages) have so considerable an expansion beyond the limits of their nutrient vessels, and derive their blastema through such a length of imbibition, that it is almost metaphorical

to talk of their supply of *blood;* and in the second place, I wish some stress to be laid on the fact, that the additional blastema which is furnished under such circumstances of local requirement, is *developable*—is susceptible of organic transformation and growth; for this fact marks an important distinction between it and the fluid, in other respects very similar, which is exhaled under the influence of passive hyperæmia.

It may be convenient that I should remind you of some of the cases in which this arrangement is illustrated. The *use of an organ*, in proportion as it is intense and long continued, occasions an additional abundance of blastema to exist in that organ, as is evidenced by the greater rapidity with which the elements of the organ are reproduced. A *mechanical injury*, such as a torn wound of the skin and areolar tissue, is presently succeeded by redness and swelling, accompanied by the exudation and discharge of a fluid, in which the microscope recognizes an abundance of newly organized cells, growing out of the excessive blastema which has been furnished; slighter mechanical injuries, such as *continued friction* of a portion of the skin with hard instruments, will presently cause the cuticle to be elevated (though unbroken) by an increased blastematous exudation from the surface of the cutis, forming what we know as a blister. Many *chemical injuries*, such as the application of ammonia or cantharides, notoriously work similar results; so do extreme *heat* and extreme *cold*.

The changes which these several causes determine in the molecular construction of parts, may probably be generalized as *wasting* or *destructive changes;* and it is under the influence of these destructive changes, that the arrangement to which I have referred comes into requisition, and the affected parts become saturated with blastema, sufficient, or more than sufficient, for their repair or renovation.

The next step towards precision in this matter consists in the statement that this excess of blastema *in* the tissue depends on an increased afflux *to* the tissue; that it consists of exudation from the nearest bloodvessels, and is accompanied by their greater turgescence and fulness: that its occurrence is determined by some condition equivalent to increase of pressure; and that (unlike that which occasions the effusions of passive hyperæmia) it is not accompanied by the counter-pressure of any distal obstruction to the escape of blood.

Then, thirdly, comes the doubt—if there be an increased afflux of blood to the part, in which of two conditions does this afflux arise? Does it arise in a direct attractive power exerted by the part on the blood, so that this fluid is drawn together more vehemently than usual? Or is there something like reflex action in the case? Is an impression of the local destructive change conveyed to the centre, and then responded to by the transmission of more blood to the part, in a method of operation which implies the agency of the nervous system? And, fourthly, in the latter event, what is the exact

nature of the change thus induced in the afferent bloodvessels of the part?

Under both suppositions, I imply that the change in the molecules of the part is the first step of the process. In cases of mechanical and chemical injury, it is obviously so. In the primordial development of parts, we are able without difficulty to satisfy ourselves, that organs which subsequently become dependent on bloodvessels do at first grow quite extra-vascularly; and that the prolongation of bloodvessels into their substance (a change which, relatively to their previous state, may be called a hyperæmia) only occurs after they have reached a certain maturity: so that, if we were to use terms implying the relation of cause and effect between the intimate structure of such organs and their vascularity, we might speak of the structure as determining the vascularity, but by no means of the vascularity as determining the structure: we might speak, for instance, of the ossification of cartilage occasioning its permeation by bloodvessels, since it begins to ossify before it begins to be vascular; but we could not reverse this, and speak of the structural change being determined by the greater vascularity of the cartilage. The change of molecular structure determines the change of vascular supply.

Guided by this analogy, we are able to draw a similar inference respecting some of the hyperæmial changes which occur in secreting organs: if you remove one kidney, so that there may remain an insufficiency of glandular substance for the excretion of urine, you presently find that the bloodvessels of the remaining kidney have become larger, and that the number of glandular elements in this kidney have likewise become vastly multiplied. Now (so far as we know anything in physiology) we know that the abundance of cell-growth in an excreting organ is an immediate consequence of the presence in the blood of certain matters which it is the function of that glandular cell-growth to eliminate. We are accordingly led to consider the enlargement of bloodvessels as a secondary phenomenon, subsequent to the multiplied cell-growth, necessary to maintain it, and essentially analogous (as I have hinted) to the process by which bloodvessels were originally given to the embryonic organ, only after it had undergone the first steps of its development.

I may take this opportunity of making two other remarks, as explanatory of our present subject. First, no variation in the *action of the heart* can account for any distributive inequalities of circulation: the heart acts as a forcing-pump for the whole body equally; it maintains all the vessels in a state of similar repletion; it can contract more forcibly or less forcibly than usual—can give much impetus or little impetus to the circulation; but what it does for one organ, it does for all; it can show no preference—can do no more for organ A than for organ B or C; any more than a change in the water-level at the New-River Head can stop the supply of No. 1 in a street, while it floods the premises of No. 2. And secondly, the property of mere *elasticity in arteries* would not account for the phenomena of unequal distribution of blood. Elasticity, no doubt, exists to a great extent

in arteries, and it fulfils very important uses: by maintaining constant pressure on the blood within the large vessels, it converts the successive impulses of the heart into a continuous circulation of blood; so that when you look at capillary circulation (in the frog's foot, for instance) you do not see it proceeding in successive jerks at each beat of the heart, but running smoothly, evenly, continuously, and never varying. But it will be obvious to you that elasticity can only give to arteries the faculty of adapting themselves to their contents—the faculty of exerting a counter-pressure on the blood proportionate to the heart's pressure; and that this faculty, or rather this physical property, is not subject in its manifestations to the laws of vital excitability. No physical property akin to elasticity would account for the conjunctiva becoming red, when you put a grain of capsicum into the eye.

The alternatives which I just implied, as regards the afflux of blood to the inflaming or over-growing part, admit (as I have stated) of being put thus: (1) More blood is *attracted* to the part in consequence of the molecular changes advancing there, and the hyperæmia results directly and immediately from an influence exerted by the changing tissues on the circulating blood; or (2) by indirect means, (such as the nervous system would supply,) a modification occurs in the *impulsion* or *admission* of blood, and the hyperæmia must be considered a reflex phenomenon.

Perhaps there is partial truth in both of these suppositions; but it is not possible to examine them fairly without entering somewhat on the structure and function of arteries, and considering generally the nature and extent of influence exerted by the nervous over the vascular system.

1. It is certain that the arteries (and in some animals the veins likewise) are muscular organs; that they are capable of effecting changes in their own caliber, and consequently of affecting the nutrition of parts beyond them in the circulation. The muscularity of arteries, of which John Hunter made physiological proof, is now a matter of eyesight. The greater part of what is called the middle coat of an artery consists of fibres—not, indeed, striped and encased in limitary membrane, like those of voluntary muscle, but of fibres essentially similar to those of the urinary bladder, of the intestines, of the dartos; fibres, forming a link in that chain of transition by which muscle gradually declines into contractile areolar tissue. That this tissue possesses inherent irritability has been shown again and again by its contraction under direct mechanical stimuli, and by its susceptibility to cold. The complete emptiness of arteries which we commonly find in the dead body depends on the final exertion of this contractility under the influence of the *rigor mortis*, an exertion by which their contents are propelled into the veins. Surgically, we all know how arteries contract when they are cut asunder; and, though part of this contraction is no doubt due to elasticity, and is a mere collapse from the withdrawal of that dilating force which the circulation previously exercised, yet we are able in other cases to see arteries palpably lessen their caliber, (even when they are full

of blood) in consequence of mechanical irritation and exposure to the atmosphere.

Schwann performed a very neat experiment, showing the latter quality more exactly than had previously been done; though, of course, the contraction of bloodvessels under the influence of cold has been known to the Medical Profession from time immemorial. On one very hot day, furnished with some very cold water, he brought the mesentery of a living frog into the field of a microscope, and adjusted his focus to an artery of about $\frac{1}{15}$ inch diameter. He then let the cold water fall drop by drop on the membrane, and presently found the artery contracted to a third of its previous diameter. He desisted from the application, and in half an hour the artery had resumed its former size. He then again reduced it by cold; and he continued for some time thus alternately making the artery contract and letting it dilate, just as you may do with your iris in alternately turning your eye to light or shade. The experiment is a good one, because it is so precise.

The brothers Weber have demonstrated that the muscular coat of arteries is susceptible to electro-galvanic stimulation. By passing a current through small arteries (diameter $\frac{1}{80}$ to $\frac{1}{200}$ inch) in the mesentery of frogs, they have found that within a few seconds a contraction ensues, which reduces the canal of the artery to half its previous capacity; and that a continuation of the same stimulus would by degrees completely obliterate the vessel. This contraction confines itself exactly to the portion of the artery stimulated, not extending itself (if the operation be neatly performed) beyond so much of the artery as lies between the wires. The contraction does not begin suddenly at the moment of completing contact, but gradually a few seconds afterwards, and may go on augmenting itself for some time after the contact has been broken. After a little while (provided the stimulation have not been excessive), the artery recovers its former capacity, and is liable to present again the same phenomena, on a repetition of the experiment; but if the current have been too powerful or too long continued, the artery will for a while have lost its muscular tone, and will not only refuse to contract again under the current, but will yield to the pressure of the circulation, so as to present an aneurismal bulging.

Professor Paget, in the admirable lectures which he recently delivered at the College of Surgeons, drew attention to a case in which the irritability of arteries and veins may still more easily be demonstrated in warm-blooded animals. He stated that, under a very slight amount of gentle friction, any small artery and vein in the web of the bat's wing would gradually contract at the irritated point till their canals became quite obliterated, and would then gradually expand again, as in Weber's experiment, to their former or to still greater dimensions. By his kindness, I have been enabled to verify this; and I have likewise been able to observe similar changes in the mesenteric vessels of the frog.

2. With respect to nervous influence—there is unquestionable evidence that the nervous centres affect and modify the movements

of the heart; and that parts receive more or less than their usual supply of blood, under influences which are purely nervous.

First, we know that the *heart* may be affected through the nerves. The most familiar illustrations are those of a mental affection, quickening the pulse; but there are instances of an opposite kind, equally conclusive in their way.

It is quite true that you may cut out the heart of a living frog, and that it will continue beating as rhythmically in a glass of water* as just before it did in the pericardium; but this does not alter the fact that—when the heart is in its natural relations, and when its ganglia have their natural commissural connections with other parts of the nervous system, its pulsations are accelerated or retarded by influences of a purely nervous origin.

For instance, Professor Weber finds (and the observation is one of the most striking with which I am acquainted) that if he sends a galvanic current through the medulla oblongata of a frog, the heart's action is instantaneously arrested, or, if not arrested, is retarded to a very remarkable degree; sometimes the one, and sometimes the other. One of his experiments stands as follows: Having cut a frog asunder, so that the spinal cord was removed below the cervical region, while the heart and lungs remained in connection with the head and medulla oblongata, he counted the beats of the heart, they were 36; he passed the current transversely through the medulla oblongata during a minute, the pulsations fell to 8; he stopped the current, they again rose to 36; and, on his once more completing the circuit, they again fell to 8, from which they subsequently rose to the original 36.

It is likewise beyond doubt that partial irregularities in the distribution of blood are produced under the influence of the nervous system. The flushing of the face with mental emotion is an instance of this; the same emotion may have excited the heart, but (as I have already explained to you) no excitement of the heart can cause partial distributions of blood. There must be some cause peculiar to the part, to account for its receiving more than its share of blood; if the heart were the sole agent in producing the effect, it ought to be produced in all parts of the body equally; we should blush all over. Erection of the penis is another phenomenon of local hyperæmia, notoriously dependent on nervous influences; and in this case the immediate importance of the nervous system to the production of the hyperæmia has been shown by experimental evidence; for after division of the pudic nerves (according to Müller), the penis loses its faculty of erection.

With respect to the manner in which these irregularities of distribution are produced, there are no conclusive experiments evincing visibly that the muscular coat of the artery is under the direct con-

* There is a fallacy, too, in the above experiment; or, rather, it does not at all prove that the heart is independent of nervous influence; for the ganglia are in immediate connection with the heart; and if this organ, when removed, be cut across, it will be found that the basial half (still in connection with its ganglia) will continue to contract rhythmically, while the other half (now quite dissevered from nervous influence) will remain motionless.

trol of the nervous system. Valentin's experiment (in which the thoracic aorta appeared to contract while the thoracic ganglia of the sympathetic were undergoing stimulation) has not had its results confirmed by other observers. Analogy would justify us perhaps in assuming it as probable, since nervous fibrils are distributed to the tissue in question, that it (like all other specimens of the same tissue distributed in the body) should be under direct nervous influence; but there is a total want of evidence as to the nature and extent of that influence. In the lower animals, one may occasionally see something that seems likely to bear on the subject; in the leech, for instance, when you expose the dorsal vessel, you see it pulsating—and not only it, but the branches likewise which are derived from it, with a regular systole and diastole; and if you snip across the vessel at two points half an inch asunder, you see the intermediate bit of vessel, though now quite empty of blood, continue its former rhythm of movement uninterruptedly; but if you detach the vessel from its lateral connections, even without cutting it across, if you isolate it completely from the ganglia which supply it with nerves, every trace of contraction ceases at once and forever. Still, in attempting to apply this analogy to the functions of higher animals, we must not neglect two points which materially affect the conditions of such analogy; first, that the muscular structure of the leech's dorsal vessel is of a much higher development than that which exists in the arteries of the vertebrata; and secondly, that from this reason, and from the absence of a true heart in that animal, we ought perhaps to compare the contractile vascular system of the leech to the heart, rather than to the arteries, of more highly-organized animals.

There is some evidence making it probable that the nutrition of parts depends, for its quantitative variations, on impressions conveyed to the nervous centres by centripetal or sensitive nerves, and responded to by changes (whatever those changes may be) which induce active hyperæmia. The disorders of nutrition, which arise as consequences of disease or injury operating on the trunk of a sensitive nerve, seem to me an indirect but forcible testimony to this point. It almost seems, in such cases, as though Nature formed a misapprehension of the state of the part in consequence of wrong intelligence being transmitted through the diseased nerve; and as though she acted on that misapprehension according to her normal course of proceeding. A sensitive nerve conveys to the centre, where it terminates, a representation of the state of those parts where its fibrils commence, and can convey no other impression; a portion of the ulnar nerve commences in the integuments of the two innermost fingers, and terminates in the brain; it conveys impressions corresponding only to those fingers; and, whether you excite the nerve where it begins in the hand, or where it terminates in the brain, or at any intermediate inch of its line of telegraph, you can produce in the consciousness of the individual no other impression than that of sensation in his two fingers. Hit your "funny-bone," and you can hardly divest yourself of the conviction that the fingers themselves have been struck. Gradually, we become accustomed to this illusion;

we recognize it as a misapprehension, inseparable from the arrangements of our nervous anatomy. Yet, strange to say, Nature will sometimes act on that misapprehension; and the distant uninjured part will become the seat of hyperæmia. Several years ago, I was consulted, at King's College Hospital, by a man who some months previously had torn his ulnar nerve at the inner condyle; his *two inner fingers had become swollen and livid with vascular injection.* Two years ago, I had a female patient here with disease in a large portion of the lumbar and sciatic plexus of nerves on one side, causing paralysis and anæsthesia of the limb; neuralgia was referred especially to the vicinity of the knee; and at this spot (when I first saw the patient) *ulceration had occurred.* It has long been known that injuries or diseases of the ophthalmic division of the fifth nerve lead to alteration in the nourishment of parts where the radicles of that branch arise—to injection of the conjunctiva, to opacity and subsequent ulceration of the cornea, and often to final destruction of the globe of the eye. In a case of the kind, which I saw with Mr. Dixon, some years ago, (and which he has reported in a very instructive form in the *Medico-Chirurgical Transactions* for 1845,) there was likewise *ulceration at the cutaneous source of the nerve* at the inner canthus of the eye, and at the ala nasi. Similarly, it is known that the nutrition of the lung is gravely affected by injuries or diseases of its sensitive nerve, the pneumogastric; experimental division or bruising of these nerves (if the animal survive the operation) never fails to induce true pneumonia—that is to say, not mere congestion of the lungs, but the development of new products.

Now, in all these cases, observing that *sensitive nerves* are the seats of lesion, and considering the known functions of those nerves, it is difficult to avoid the conviction, which I have already suggested, that the *modus operandi*, by which such diseases and injuries are enabled to produce distant inflammatory changes, consist in a reflex operation on the bloodvessels; that a false impression of the state of distant parts is conveyed to the nervous centres by the disease of their incident nerve-tubules; and that this false impression determines a change in the vascular supply of the part where the nerve-tubules take their origin.

Endeavours have been made to found an entire theory of active hyperæmia on phenomena such as these. It has been argued, that the first impulse to its occurrence is in the form of a sensational change—that the causes of inflammation act on the extremities of sensitive nerves in the parts exposed to injury—that a nervous centre is then excited—that a motional impulse of some sort or other is reflected to the muscular coat of the artery, and that thus the affected organ becomes the seat of a vascular repletion. It is admitted, I believe, by the holders of this view, that idiopathic changes in the same nervous centres may exist, as an explanation of such acts of hyperæmia as do not arise in exterior local impressions.

Now—that *the first change* in the inflaming or overgrowing part is a nervous change, leading to the determination of blood, is a position which I may venture to deny; at least, as regards the *modus*

operandi of all exterior irritants. It is notorious that paralyzed parts are susceptible of artificial irritation, and become inflamed. I have made many observations on the subject, and have noticed that the absence of a spinal cord, or the division of all the roots of the nerves, or the section of the lumbar and sciatic plexus, will make little or no difference as to the certainty with which an irritant applied to the web of a frog's foot will quicken the circulation there, and subsequently lead to its retardation and arrest.

Perhaps the neuro-pathologists might object here, that we do not accurately know what are the branches of nerves—and still less what are the nervous centres, determining muscular movements in the arteries; and that, in the experiments just cited, some essential element for the nutritive innervation of the part (*i. e.* for the supposed function of its artery) might have been left uninjured.

There is, however, little room for fallacy in the experiment which I am now going to tell you. A patient had complete anæsthesia of the fifth nerve, dependent (as a post-mortem examination subsequently showed) on its organic disease; the conjunctiva, as well as the integument of the face, was utterly insensible; not only was the function of the nerve destroyed, but those reflected nutritive changes of which I have already spoken had taken place, and had exhausted themselves; showing that the nerve was spoilt for participation in the acts of nutrition (whatever they may be) no less than for its more obvious uses as a medium of conscious sensation; the cornea had undergone ulceration, and had healed again. The following experiment was carefully made: The lids being held open, a single granule of cayenne pepper was laid upon the insensible conjunctiva; in a few moments, it had become the centre of a very distinct circle of increased vascularity, the redness of which slowly became more and more distinct as long as the stimulus was suffered to remain; so that, on its removal, there was a very evident circumscribed erythema on the surface of the membrane. I consider myself justified in believing that this change occurred without any intermediate nervous excitement; not only because the history of the case would lead me to consider the fifth nerve as annihilated; not only because the experiment was totally unattended with sensation; but likewise because there was the very remarkable absence of that sympathetic phenomenon, which the faintest remnant of nervous excitability would have produced—namely, there was not the slightest trace of lachrymation.

Altogether we may, I think, take it as an established certainty, that the first change which occurs in an inflaming or overgrowing part, and which leads to its becoming loaded with blood, is not a reflex change operated through the nerves, but is a direct change operated by the living molecular structure of the part on the blood which traverses it, or on the vessels which convey that blood. "*Ubi stimulus, ibi affluxus*" will stand, then, as a law of reciprocal relation between the solids and fluids of the body, which does not of necessity require the intervention of a nervous system for its initiation.

Thus much as regards the first momentum of the process;—a momentum which is apparently independent even of the specific endowments of the artery; seeming, as one watches its occurrence, to arise almost as though there were a vortex established in the place of the irritant, causing all the adjoining streamlets of blood to converge in swifter currents towards it.

In ulterior stages of the process, however, something else may be observed; and of this I shall speak in my next lecture.

LECTURE V.

Active hyperæmia (continued); condition of afferent vessels; reflex-relaxation? increased action?—Irregular growth. (1) Hypertrophy, its distinction from inflammation, and from various accidental causes of increased dimension; laws of repair after waste; hypertrophy of muscles; of gland—nephritis, bronchocele; reparative hypertrophy—rickets; hypertrophy from withdrawal of pressure—cranial bones, teeth. (2) Atrophy; from disuse of organs; muscular; osseous; glandular; relation to local anæmia; progress and mode of origin of atrophic changes; accidental atrophy from disease of arteries; brain; kidney; effects of secale cornutum; pressure—difference in its effects, as it is constant or remitting. (3) Morbid changes of consistence, and their relation to changes of nutrition.

Gentlemen: Towards the close of my last lecture, I showed you reason for believing that the *initiation* of the inflammatory process is independent of nervous influence—that it occurs by virtue of some law regulating the molecular growth of the invaded textures, and in immediate consequence of changes in their organic condition—that these changes (whatever may be their method of operation) are competent to affect the stream of capillary circulation; first, to quicken and narrow it; next, to widen and retard it; finally, to solidify and arrest it. These affections of the stream are accompanied by the extra-vascular effusion of fluid which naturally belongs to the intra-vascular blood; an excess of *liquor sanguinis*, more or less diluted, makes its appearance amidst the elements of the affected tissue. Whether it be in this way that the first momentum is given to changes in the local circulation—whether, namely, the first alteration in the capillary currents be due to an excessive exosmosis provoked by changes in the tissues, and leading to intra-vascular obstruction as a result of inspissation of the blood there—this is a point on which my present knowledge does not allow me to give you any certain information.

I will not venture to travel in this direction further than the conclusion to which I have led you, that the inflammatory process (like most other vegetative or nutritional changes in the body) commences independently of nervous influence, as a change primarily manifested in the organic molecules of the part, and relating to their ultimate conditions of life and growth.

I have told you that active hyperæmia ensues on a variety of local changes. So invariably does it attend those which I have just spoken of, that inflammation is often described and defined as an increased action of the vessels of a part; and we are apt at times to forget, what I have endeavoured to point out to you, that the altered action of the part is prior to the increased action of its vessels.

Now, as regards that increased action, the bare facts of the case are as follow. Under the influence of some developmental impulse

in a part, (such as that which originates the process of hypertrophy in a kidney, in a muscle, in a uterus,) or under the influence of those local changes which we have been considering as primordial in the inflammatory process; but, equally in either case, under the influence of a change which is local and peripheral, there occurs an enlargement of the bloodvessels leading to and leading from the part which is the seat of change; there occurs an ampler circulation of blood through the part.

Our knowledge of the physiology of the bloodvessels permits us to interpret this phenomenon in but one way. It is an *act of relaxation* in tissues which are irritable and contractile. We know that arteries can diminish their distribution of blood only by lessening their canals: we know that they can increase their distribution of blood only by expanding their canals. We know that their muscularity enables them to achieve either of these purposes; the former, by muscular contraction comparable to spasm; the latter, by muscular relaxation comparable to paralysis. The last word is in some respects a startling one, as referable to these sympathetic processes; but Hunter applies it to the state of hyperæmial vessels; and the neuropathic theory of inflammation is entirely founded on the reality of such a state. Inflammation (argues Professor Henle) is a phenomenon of the excito-motory class; the peculiarity in its development is this—that, whereas it is the general rule of muscles which act under reflected stimulation, that they *contract;* there is a contrary law for the muscular coat of arteries, to the effect that, under reflected stimulation, it becomes *relaxed.* I would venture (as I have stated) to hesitate in accepting this as a true statement of *the first act* in the drama of inflammation; but, with this reserve (a reserve which extends only to placing it in the second, rather than in the first series of inflammatory changes) I may tell you that it seems to me the only plausible explanation of the condition of the larger bloodvessels in active hyperæmia, whether inflammatory or hypertrophic.

There are some facts, and especially some considerations of analogy, which would lead one to study very curiously whether the artery takes any active share in the propulsion of blood under these circumstances. Observation of its muscular structure and contractility, a familiarity with the rhythmical movements of the heart from which it is distributory, a knowledge of instances (down the scale of organization) where very similar vessels make rhythmical pulsatile contractions—these points make one suspicious whether there may perhaps, during health, be latent in the arteries of the higher animals a capacity for action like that which is obvious and energetic in the dorsal vessel of the Annelida; latent during health, but liable to be excited into activity and manifestness under abnormal circumstances: a capacity for alternate closure and expansion, analogous to, and synchronous with, the systole and diastole of the heart; a function by which the artery would be enabled to receive more amply, and to propel more vigorously, whatever amount of blood the local changes might require.

Some such hypothesis as this (implied at least, though not always

very clearly expressed) seems generally to prevail, in this country, as an explanation of the phenomena of determination of blood; and I may confess that, when first I proceeded to test it experimentally, I began my inquiry with some expectation of arriving at an affirmative result. It was a plausible theory; it seemed accordant with the general physiology of the vascular system; it pretended to show that sort of increased effort of nutrition—that synergic activity of bloodvessels, which one was prepared to anticipate under the conditions of inflammation and hypertrophy; and moreover, it stood as the alternative of an *à priori* improbability; for it promised to supersede the necessity for admitting that very striking anomaly in the laws of muscular contraction to which I have already adverted as the *reflex-relaxation* of stimulated arteries.

After many examinations, however, I have never seen anything which could give support to such a view. Again and again, I have had under my eye the arteries leading to a focus of inflammatory action; sometimes I have excited the inflammation while the afferent artery has been under the microscope; sometimes the irritant has been applied several hours previously; sometimes, by ligature of the aorta, I have isolated the artery from the influence of the heart, so as better to observe its peculiar share in the phenomena; but under none of these circumstances have I ever succeeded in observing anything like rhythmical contractions in the vessel.

Not only have I failed to observe such contractions, but I have seen very distinctly the generation of a symptom which they have been supposed to produce, and which apparently they do not produce; I mean, throbbing. I have traced an artery, have watched it branching to inflamed and to non-inflamed parts, have seen the outlines of its muscular coat absolutely without movement, and its caliber quite uniform; but the large branch which led to the seat of inflammation, being expanded so as to oppose a minimum of resistance to the circulation, suffered the stream at each beat of the heart to strike with a direct and visible shock on the contents of the smaller and obstructed vessels which surrounded the area of disease.

I think, gentlemen, it would be rash, in the present very imperfect state of our knowledge, if I should pretend to offer you any complete pathological theory of the origin and progress of the inflammatory and hypertrophic processes. As yet we possess but fragments of the subject, and can show little more than the first indications of a theory. So far as those indications go, I may recapitulate the following points as *probable* conclusions in the matter:—

(1) In the chain of events which terminates in hypertrophy or inflammation, the first act relates to the influence exerted by the elements of the part on the materials of the blood circulating through it, and consists in an alteration (perhaps in hypertrophy only a quantitative alteration, possibly in inflammation also a qualitative alteration) in those changes which the part naturally works on the blood, as the indispensable condition of growth. The growing elements of the part—hurt by physical violence, or affected by extremes of temperature, or thrown into rapid chemical changes, or over-

burdened with their own specific stimuli from the blood—strive to grow more, or to grow differently, than in their previous state. The sudden origination of this effort (as it occurs, for instance, after mechanical injury) suffices apparently in itself to derange the currents of the capillary circulation, to flood the tissue with serous exudation, and to lead to those microscopical phenomena which are considered pathognomonic of inflammation.

(2) The condition of a part in which the organic changes are thus accelerated (whether in the form of hypertrophy or inflammation) is capable of inducing, in the muscular arteries which lead to it, a state of enlargement or increased perviousness, which determines to the part a larger afflux of blood; and it is in a high degree probable that the manner in which this enlargement occurs is by the way of what we technically call *reflexion;* that a certain impression from the part is conveyed centripetally by its sensitive nerves, and is responded to by a return-current through the motory nerves of its artery; that the specific influence of this return-current is to induce a relaxed condition of those muscular fibres, which regulate the caliber of the artery, and by this relaxation to suffer an increased transit of blood to the inflaming or overgrowing part.

We have next to inquire, what are the chief results which may arise in a part from an augmented determination of blood thither? —what are the chief consequences of active hyperæmia? They vary most importantly according to the following differences: (1) The determination of blood, though over and above the usual supply, may *admit of application* according to the ordinary and healthy functions of the part. The biceps muscle of a blacksmith's arm receives perhaps as much blood as all the muscles of my upper extremity put together; but there is no blood wasted; all that goes there is turned to account, and contributes to the increased development of a normal tissue. Or, (2) the supply of blood may be *more than can be used* and appropriated by the organ so copiously supplied; and then it is that we get a continued superfluity of exudation pervading the tissue, and find that superfluity undergoing an independent development into certain shaped products—cells or fibres—foreign to the healthy structure of the part.

Now, what I have just stated is the distinction between hypertrophy and inflammation; their general pathology has much in common —their causes are often alike—their modes of production identical. But in hypertrophy—however large may be the supply of blood, it all goes to the true nourishment of the organ, goes to increase the number of its natural molecules; while, in inflammation, all that is redundant goes to the formation of new products. After what I have said of the pathological affinities of these two processes, it will not surprise you to be told that in many organs of the body hypertrophy and inflammation run into one another by almost insensible gradations—as, for instance, with secreting surfaces, where, after a certain time, that which produced at first a mere excess of secreted material presently causes to be mixed with that secretion more or less albumen, fibrin, blood, pus, and the like.

My next lecture will be mainly occupied with an account of the development of these inflammatory products; therefore, for the present, I shall pass them over without other notice, and shall confine myself to such fluctuations of nutrition as are not accompanied by development of new tissue. And, in commencing the separate consideration of hypertrophy, let me first of all warn you to distinguish real hypertrophy from such as is only apparent. An organ is not hypertrophied, necessarily, because it has a greater number of square inches in its surface. Let me give you a few instances of this. A man with cirrhosis, or some other obstructive disease in the liver, may have an immense spleen; as you percuss over his left hypochondrium, you find six times the legitimate extent of dulness; but if you should impute this enlargement to hypertrophy, you would make an error; it consists simply in distension of the venous cells of the spleen by accumulated blood; it is passive hyperæmia in a very distensible organ. So, also, when in making examination of a paraplegic patient, you find a great sac of urinary bladder rising up to the umbilicus—this is not hypertrophy of the bladder, but distension of it, by accumulation of its natural contents. So again, in parts of the skin where there are sebaceous follicles, it is a very common thing to find the orifice of one obstructed; and then, if the secretion goes on, a cyst is formed; such is the origin of common follicular tumours of the scalp; and although, in their advanced growth, these are not likely to be spoken of as hypertrophied follicles, yet where they are smaller and several in number (as on some mucous surfaces) the erroneous application of the word *hypertrophy* is not very unusual. Take care, then, not to say that parts are hypertrophied, when they are simply distended and spread out.

Secondly, it is a very common thing to find the word *hypertrophy* inaccurately applied to organs, which are increased by some foreign deposit, whether inflammatory or not. Thus, hypertrophy of the tonsils is spoken of; whereas the disease so called consists, I believe, partly in a filling of the follicles, and partly in thickening of the surrounding cellular tissue with products of inflammation. Again, hypertrophy of the labia and nymphæ is sometimes spoken of as a result of gonorrhœa and dirtiness; the real fact being, that the skin, which becomes pendulous under these circumstances, has previously been distended by inflammatory œdema, and has subsequently retained a chronic interstitial thickening. The same error of overlooking inflammatory deposit is sometimes committed in examinations of the intestinal canal; a portion of thickened stomach or bowel being said to be hypertrophied, when the real disease consists in an inflammatory development in the substance of its submucous coat. So, the second caution I have to give you is, that you will not let the word hypertrophy include enlargements or thickenings which depend on the deposit and growth of foreign material.

Coming, then, to real hypertrophy, we may define it as the multiplication, or magnification, of normal elements; the exaggeration of a tissue, or of an organ, in its own particular type. For instance, take a large liver; I repeat, that you would not call it hypertrophied

for being full of blood, or for having a quantity of serum or lymph effused through its substance, or for being stretched and bulged by an abscess or hydatid cyst in its interior; but simply and singly you call it a hypertrophied liver, when it has got more *liver* than it ought to have—more of that very stuff for which you call it liver, rather than muscle or skin.

And now—Under what circumstances does hypertrophy occur? What are its causes?

It may, I think, be stated as a general fact in the economy, that if the nutritive conditions be perfect, if the blood and the organs be what they should be, whenever the active structures of the body renew themselves, they do that and something more. Nature gives them enough for their exact necessity, and for something beyond it; they renew themselves more largely and luxuriantly than in their original construction.*

Of this general fact, or law, I can give no causal explanation: I cannot say what makes it be so; but its purpose is obvious, and it brings before one vividly that *vis medicatrix naturæ* which the older physiology delighted to speak of, watchfully strengthening every part of the organism in proportion to the stress upon it, and always contriving that no active portion of the system shall become languid for want of sufficient renovating material.

But, whatever may be the explanation of the fact, it seems to me the expression of a law including all the chief cases of pure hypertrophy. In all such cases, if you look carefully into their whole pathological history, you see what may be generalized as a vigorous reaction against waste, a reaction which, in every case, as I have said, seems to go somewhat above the exact quantity of repair and restitution due to the part; and which, when it extends over sufficiently long periods of time, is able to accumulate its effects as a permanent overgrowth of the affected tissue.

The chief heads under which you may consider the subject of hypertrophy are the following: hypertrophy of muscle; hypertrophy of glands; reparative hypertrophy.

1. Muscle grows exactly in proportion to its exercise; and this is true, not only of the voluntary muscles, such especially as those of the limbs, but even, still more remarkably, of the involuntary muscles. See, for instance, in the heart; where any obstacle has opposed itself to the circulation of blood—where the mitral orifice has allowed regurgitation—where the aorta has been rendered rigid by calcareous deposit, or where its origin has been obstructed by fibrinous concretions—how immensely the muscular substance of the ventricle increases in its thickness and in its power. Or observe

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* Supposing, for illustration, that so often as x grains of old tissue are consumed in certain acts of exertion, $x+a$ grains of new tissue are ready to be substituted for them; then (putting arbitrary numbers aside) we should infer, that organs in active exercise would continually and progressively grow during life. And, in point of fact, such appears to be the case. "M. Bizot and Dr. Clendinning have proved of the heart and arteries, which are thus constantly exercised, that their average size regularly increases (though with a decreasing ratio of increase) from childhood to old age, provided only the old age be a lusty one."—*Paget's Lectures*, Ser. I., p. 23.

the bladder, where enlargement of the prostate gland, or the presence of a calculus, or the permanent impediment of a strictured urethra, has interfered during many years with the process of urination, and you will find that the increased labour thus thrown on the muscular coat of that hollow viscus will have caused it to become hypertrophied to several times its normal thickness.

2. The hypertrophy of secreting glands has been very much overlooked, for what is now an obvious reason. A gland may be materially hypertrophied without being larger than its normal size; it may merely be denser than natural. The essential phenomena of the disease are only to be followed by the microscope; but they deserve the most attentive study; for it is particularly in respect of glands and secreting surfaces, that I would beg you to remember what I have already mentioned—that, under certain circumstances, their hypertrophy runs to inflammation, and produces destructive consequences. Thus, in that more common form of Bright's disease which I have described, in the *Medico-Chirurgical Transactions*, under the name of subacute nephritis, there is an initiatory stage, in which it is difficult to pronounce whether the organ be in a state of hypertrophy or of inflammation: that is to say, there are none but normal elements present—nothing but a profusion of the natural cell-growth; and if it were not for the previous presence of albumen in the urine, or perhaps for finding a few of the Malpighian bodies injured by the hyperæmia, one might almost speak of the disorder as a mere hypertrophy in the secretive structure of the gland. The same is the case, too, in respect of the early stage of cirrhosis of the liver. It may be observed, that the causes which produce this redundant cell growth in the glands, and which eventually excite inflammation in them, are precisely what are called their specific stimulants—i. e. such ingesta, or such products of digestion, as excite them to secretion. As the waste of a muscle is in contracting, so the waste of a gland is in secreting; and thus, according to the universal law, excitement of the secretory functions leads to hypertrophy of the secreting structure. Among materials which excite the glands to their characteristic manifestations, and which may be called stimulants of the gland, none are more energetic than those very substances which the gland ought to eliminate. Nothing can more thoroughly dispose a gland to action, and therefore nothing can more predispose it to ultimate hypertrophy, than an increased accumulation in the blood of those particular materials which the gland should appropriate to itself for secretion. Hence, no doubt, it is that, when one of two symmetrical glands has been removed, its fellow undergoes a slow hypertrophy, so as to do compensative work; for the stimulant material in the blood, which originally divided itself between two outlets, now concentrates itself on one; increasing first of all its waste, and subsequently its nutrition.

The thyroid gland, in the disease called *goître* or bronchocele, often (if not always) presents at its commencement a pure hypertrophy in the secreting structure. You are probably aware that the natural arrangement of this organ is in closed vesicles, lined, not

by nucleated cells, but by simple nuclei, partly applied to the walls of the vesicles, partly floating in their fluid contents. Now, when hypertrophy begins here, these nuclei undergo a higher development, and give origin to large transparent cells, which fill and distend the limitary membrane of the vesicles. Analogy would justify the suspicion that whatever exterior influences produce this endemic disease must stand in some peculiar relation of chemical affinity to the natural intra-vesicular secretion of the gland, and that thus (principally, if not only) they would possess their power of stimulating the organ to increased efforts of secretion and growth.

3. As respects the reparative process, I may give you one or two illustrations of the general doctrine of hypertrophy; as, for instance, this; that in the mechanical structure of the body, where disease or accident has either weakened a tissue, or has thrown augmented stress upon it, its reparation generally becomes hypertrophic.

We very commonly see this illustrated in the skeleton. If the tibia or fibula be partially removed by disease or by experiment, that one of the two bones which is left is apt to undergo a kind of compensative development, becoming thicker and stronger at the weakened portion of the limb. So, where recovery has taken place from rachitic curvature of the spine, we find bone deposited in various degrees of superabundance; sometimes locking the spinous processes together, sometimes expanding the surfaces of contact of the bodies of the vertebræ, or anchylosing their edges. Or, in the bones of the extremities, which have been bent by rickets in childhood, and have subsequently been repaired, we see strong ridges, thrown up along the concave aspects of the curve; and this superabundant bone is placed (as Mr. Stanley observed) exactly where the curvatures of the bones render them mechanically weaker, and where, consequently, their greatest waste of tissue occurs.

The various osseous processes for muscular insertion, and the several surfaces of bony contact in the vertical plane of the trunk, are the portions of the skeleton most liable to undergo excessive waste; the former by traction, and the latter by pressure; and they are the portions consequently most liable to quantitative errors of nutrition.

Before leaving the subject of hypertrophy, perhaps I should mention another law, though it is one of very limited application—viz., that, with some contiguous organs, mutual pressure is in so far a condition of harmonious development that the absence of one of such organs occasions some capricious growth in the other. There appears to be this necessity of mutual pressure between the brain and the bony case which contains it; and in patients where the brain has undergone a slow atrophy from disease, the skull has been found presenting a very peculiar hypertrophy, inwards; chiefly by the expansion of its diploë, so that the inner table of the cranial bones has maintained its natural contact with, and adaptation to, the shrunken convolutions of the brain. This is, perhaps, not very frequent; but in the majority of cases, where chronic shrinking of the brain has occurred, the parts show the same tendency to the main-

tenance of mutual pressure, by the effusion of a quantity of serum which occupies all the interval between their separated surfaces.

Similarly with the alveoli, it can hardly be considered otherwise than in some respects a hypertrophic process, that the alveolus, from which a tooth has been dislodged, fills itself with bone. The teeth, themselves, too, under certain circumstances, sometimes show what is rather a stimulation of hypertrophy than its reality; as you may at any time see, by removing an incisor tooth from the jaw of a rabbit. You will find that the opposite tooth, against which the removed one used to press, grows to an unusual, almost to an indefinite length, for want of the pressure and friction which formerly kept the waste of its free edge in proportion to the growth of its other extremity. Obviously, the hypertrophy is here only apparent; there is no true overgrowth of structure.

II. In *Atrophy*—the opposite condition to hypertrophy—there may be observed the converse application of the same principles as govern the latter process. In hypertrophy, you have seen the increased nourishment and increased growth of parts in proportion to the activity of their functions, in proportion to the demands made on them, in proportion to their healthy waste. In atrophy, you will see decreased nourishment, decreased growth, in proportion as there is little activity of function, in proportion as an organ is superseded in its uses, in proportion as its wear and tear in the service of the economy are slight. But, while hypertrophy rarely involves any change of tissue, beyond developing that in which it occurs to the utmost perfection,—atrophy, on the other hand, is very generally accompanied by change of tissue, and that change is a degradation and impairment.

Thus, for instance, in the muscular system, which is a very frequent seat of atrophy, you find the muscles not only becoming small and pale, in the absence of their natural excitement, but actually becoming altered in their molecular constitution. Examine under the microscope a small section of muscle from a long paralyzed limb, and you find that it can hardly be called muscle. The sarcolemma, instead of being filled with those peculiar contractile elements which are characteristic of the tissue, contains a vast number of oily globules; and these are often disposed in such lines—longitudinal or transverse—as to suggest the possibility that the original elements have actually undergone transformation into oil.

We find too that, under similar circumstances of inaction, bone is apt to atrophy. This may easily be seen in the skeleton of a paralytic limb, and sometimes in the bone of a stump. The bone, not fulfilling its natural functions, not acting as a column of support, and not being made available as the fixed point of muscular action, undergoes very little or no waste, and is consequently very imperfectly repaired. It becomes less dense and less strong than natural; its medullary cavity seems developed at the expense of its cortex, and the cortex itself seems reduced materially in specific gravity, as well as in strength.

In glands, we have occasionally the means of observing the operation of the same law: the shrinking of such as are idle or unoccupied. Such instances are chiefly furnished in the generative system. Contrast, for instance, the mamma of an old maid of fifty or sixty—an organ that has never done its natural work—with that of a young woman of twenty occupied in nursing an infant. You scarcely recognize it as the same tissue.

Probably, likewise, as respects the male animal, an equally prolonged and rigid celibacy would cause the testicles to waste from the non-excitement of their natural functions: though in the present constitution of society we seldom have an opportunity of witnessing this extreme effect.

Both with these organs, however, and with those of the special senses, Nature seems disposed to permit great exceptions to the common laws of atrophy; allowing in them such periods of perfect repose to pass without any impairment of structure, as could not occur in the organs of locomotion without very serious results. For instance, Cheselden, by the operation of couching, restored sight to a youth born blind, and who had reached the age of nearly fourteen years without relief, with an almost unused retina. Now, if a voluntary muscle had remained for so long a time in such almost complete suspension of its functions, it would probably have been incapable of resuming a healthy action. And—as respects glands, it is not a very uncommon thing to see women marry late in life, bear children, and have copious development of the mamma, although twenty years may have elapsed since their arrival at puberty, before the generative system was called into activity. It is almost exclusively in regard of the nucleated cells of glands that atrophy (like hypertrophy) shows its operation. They shrink and wither within the vesicles or tubules of the gland; sometimes collapsing, so that little survives of them but some small darkness around the original nuclei; sometimes fading and getting thinner, till they look like delicate fragments of squamous epithelium.

In all the atrophic processes which ensue on the inaction of organs, (the wasting of muscles, bones, glands, and nerves from their non-employment,) the first change produced is, no doubt, this; that they have their supply of blood progressively diminished, and that their shrinking results from their anæmia.

In the production of this change, it is probable that the muscular coat of the nutrient arteries plays an important part; contracting, to diminish the afflux of blood for organs with inferior requirements; just as we have supposed it relaxing to favour the occurrence of hyperæmia, where the organic changes of the part have been advancing with inordinate rapidity. As to the manner in which this arterial change is immediately excited, we have nothing but analogy to guide us. We have been led to believe that the occurrence of active hyperæmia depended on reflex-relaxation of the artery, in response to certain centripetal impressions denoting excitement in the organic processes of a part; and the same line of argument would lead us to suspect that organs in a condition of extreme inertia and unchange,

may originate centripetal impressions which would conduce, through nervous influence, to reflex-contraction of the artery.

The conditions of local anæmia resolve themselves under two heads: In the class of cases to which reference has already been made, the first step is the suspension of functional activity in the part, with a consequent state of molecular unchange; on this (probably by reflex contraction of the artery) ensues a diminution or suppression of the supply of blood; on this, thirdly, the shrinking of the organ. In another very large class of cases, the local anæmia occurs, not by any reflex operation, nor because of any previous inactivity of the anæmiated organ, but by means of some accidental interference with the perviousness of its arteries. You can easily conceive the effects which arise under these circumstances, knowing the absolute dependence of all growth on a due and sufficient supply of circulating blood; you can easily predict that, if by some accidental derangement of the economy, the access of blood gets cut off from organs even in the fullest discharge of their healthy functions, such organs must of necessity follow the universal law of nutrition, and suffer atrophy as the result of this accidental anæmia.

Disease of the arteries acts very frequently in this manner: An artery gets partially obstructed by atheromatous or fibrinous thickening in its interior; the parts dependent on it are partially deprived of their supply of blood, and, in proportion to their loss, they dwindle in size and development. Thus it is that we so often see that form of atrophy of the brain, which is called white softening, occur in connection with extensive disease of the arterial system: a branch of the carotid or vertebral artery becomes blocked, and the corresponding parts of cerebral substance undergo their ordinary waste without the possibility of getting renewed by a sufficient quantity of blood. And every now and then surgery gives an experimental illustration of the fact; for (as you may read in the twenty-ninth volume of the *Medico-Chirurgical Transactions*) it is not a very rare thing to see white softening of the brain follow ligature of the common carotid artery.

Senile gangrene of the extremities is another instance of atrophy and death in a part from the obliteration of its arteries.

In the kidney, too, I have observed pretty frequently a peculiar change of an atrophic nature, which arises under similar circumstances. Small knobby kidneys are common, you know, as the last phenomena in the series of changes known by the name of Bright's disease; and that nearly uniform contraction of the gland is not a consequence of the development of new tissue, as many people have supposed, but depends on the mere collapse of some of the original textures of the gland, from which a large intervening mass of cells has been slowly removed by disease. This, however is not quite the form or stage of atrophy to which I now want to direct your attention. The one I wish to allude to I can hardly mark by a better name than epithelial atrophy; for, being a comparatively rapid process, there is hardly time for its effects to show themselves beyond an arrest in the development of epithelium, or (as it ought to be

called) *endothelium* in the urinary tubules. In a large and often pale kidney, a portion of the section will appear much softer than those adjoining it; on microscopical examination, the tubes of this portion will appear quite of their natural size, and (except that the limitary membrane is peculiarly brittle) will be of their normal shape and continuity; but the interior of the canal, instead of being filled to nearly three-fourths of its dimensions with an endothelial growth, will have but a mere crust of such formation along its surface—a mere shrunken remnant of what ought to be; so that the canal in the axis of the tube appears many times larger than natural. Some years ago, examining a kidney where the tubes presented this peculiar appearance, I found what occurred to me as the explanation of the change; namely—a small artery in the specimen I was examining (the artery, as it seemed, on which the nutrition of that part had depended) was blocked completely with an atheromatous and fibrinous mass, which had probably been carried into it from some larger trunk, and had thoroughly arrested the passage of blood there. Since that observation taught me to connect the peculiar degeneration with defective supply of blood, I have been careful to examine specimens of the same kind, and again and again I have seen a similar atrophic state of the cell-growth within the tubule, where the renal artery or its chief branches showed evidence of obstructive disease.

There are many striking illustrations of atrophic diseases in internal organs, which, if time allowed, I might show you in connection with degeneration and obstruction, or inelasticity of their arteries. I will only mention to you now, that the connection of the so-called *fibrinous concretions* with such arterial diseases, and with concurrent atrophy of the proper elements of the organ, (spleen, liver, kidney, &c.,) is a very important item among such illustrations, and one that particularly invites further research than has been bestowed on it.

Perhaps I ought here also to allude to the anæmic gangrene of the extremities which arises under the poisonous dietetic influence of the *secale cornutum*, and which is said to simulate exactly the forms of gangrene which arise from arterial obstruction. The disease is almost unknown in this country, and I have had no opportunity of making any exact inquiries into its nature; but our knowledge of the action of *secale* on the muscular fibre of the uterus seems to suggest some clue for the explanation of its styptic action on the blood-vessels, and therewith for its power of producing that atrophic condition of the extremities to which I have referred. We constantly have illustrations of the extreme degree in which arterial contractions can anæmiate such parts: the phenomenon of the fingers *dying* (as it is well called) after exposure to cold, and continuing sometimes for hours in a pale and shrivelled state, is inexplicable, except as a result of spasmodic contraction in the muscular coat of the artery: and it is only a smaller and more transient degree of that anæmic atrophy which the action of secale, or any other morbid obliteration of the arteries, might more permanently produce.

No doubt it is by diminishing the access of nutrition to the elements of an organ, that pressure acts so remarkably in producing atrophy. It not only, in all probability, quickens the waste and removal of a tissue, but hinders it from being repaired again. See, for instance, how the presence of an aneurism or other tumour causes the successive atrophy of the tissues against which it presses; and see, in a cirrhotic liver, or in a lung after pleurisy, how the contraction of fibrin will operate in arresting the growth, and finally producing the starvation of the part which it invests.

But why do I say that, in these cases, the pressure acts doubly —quickening removal and hindering reparation? For this reason, that if it only quickened the removal of the tissue, there would be hypertrophy for the consequence. Atrophy only results from pressure when this is uninterupted; and if you remit the pressure at intervals, you get hypertrophy instead of atrophy as the result; because you then reduce the case to the analogy of those already described; you render it a case of simply increased waste, in the part, which is compensated for by an increased growth. Thus, instead of a tumour pressing on bone, let a surgical apparatus press there—one which is discontinued at night—and you get hypertrophy as the result. "In Mr. Cheshire's apparatus for weakness of the spine, the weight of the head and trunk is thrown upon the haunch-bones and chin. A steel hoop rests upon the ossa ilii, from the middle of which a rod rises vertically behind the spine, higher than the head, over which it arches, terminating in a hook; a strap passing beneath the chin of the patient is suspended to the hook. In those with whom this instrument has been used, the lower jaw, having to sustain unusual pressure, generally enlarges, throwing out a bony swelling at the part where the chin strap tells."* Or I may give you a still more familar instance of the influence of remission on the effects of prèssure, in reminding you of the pathology of corns. They are a hypertrophy of the cuticle, arising in intermittent pressure. Let that pressure be continual: as, for instance, no the foot of a man, whose fractured leg has been put up in a slovenly manner; and the pressure, instead of making the skin hypertrophied, and producing a corn, atrophies it, and gives an ulcer.

I must not leave the subject of hypertrophy and atrophy, without alluding to those changes in consistence which so frequently accompany them—to *hardening*, namely, and to *softening*. But these are so often compound processes, that my present notice of them may be brief. As a general, but by no means an invariable rule, hypertrophy is accompanied by some solidification of the tissue, and atrophy (as I have shown in the brain and kidney) with some rarefaction or softening. For as a general rule (and I must repeat that it has important exceptions) the larger outlines of an organ are the last to alter: atrophy and hypertrophy are essentially molecular operations; and so the one diminishes, or the other increases, the number of molecules in a given area before the area itself becomes wider or narrower.

* Mayo's Outlines of Pathology.

Before a muscle shrinks visibly with atrophy, you would find its specific gravity reduced, showing that its tissue becomes less in concentration before it becomes less in size; and so with hypertrophy, before the muscle perceptibly swells in volume, you would find its specific gravity increased as the evidence of greater molecular accumulation.

The most striking exception that occurs to me is in respect of secreting surfaces—not glands, for they follow the rule I have just stated, but in respect of simple membranes where growth takes place on a free surface. Here, as you may especially see on mucous and synovial surfaces, an overgrowth of epithelium is very generally accompanied by a softened and almost diffluent state of the product. And, to give you a different sort of exception, there can be no doubt that many atrophied organs ultimately become hard from absorption of their fluid matters and collapse of their fibrous tissue. Thus I have already noticed the contraction and hardening which ensues in the last stage of Bright's disease when all the efficient parts of the kidney have perished, and the fibrous density of a breast which has never exercised its functions, or has long ceased from their exercise. Other changes in consistence depend chiefly on serous infiltration, more or less than natural, between the constituent elements of a part; such, for instance, as we see when the brain or the lung is rendered œdematous. Or softening of an organ may depend on the diffusion of pus through its textures; or hardening may depend on the copious infiltration of fibrin, or on the deposit of earthy material in its substance. Or either may depend on certain post-mortem changes; such as the hardening of muscle which occurs in the *rigor mortis*, or the softening of the mucous membrane of the stomach and intestines after death from the presence of a free acid in them.

But all these are topics which do not now press for consideration.

LECTURE VI.

PRODUCTS OF INFLAMMATION.

I. Fibrinous effusions; ulterior changes of fibrin; collateral illustrations from anatomy of intra-vascular clots.—II. Generation of cytoblasts.—III. Their ulterior progress; pus; glomeruli—their relation to dissolution of blood; suppuration—on mucous surfaces, in solid organs; distinctions of adhesive and suppurative inflammation, and circumstances determining them. IV. Vascularity of new tissues.

GENTLEMEN: In the present lecture I purpose sketching for you the chief changes which occur in inflammatory effusions; those changes at least which lead to suppuration, or to chronic thickening in organs.

I must begin by carrying you back to the subject of my last lecture, and by reminding you of what occurs when the capillary blood-vessels are overloaded with blood. I stated to you that, under these circumstances, the capillaries suffer a certain proportion of their fluid contents to exude. I stated likewise that they change this fluid as it exudes; and that the change thus accomplished (which distinguishes the serous fluid in question from the plasma of the blood) will vary, according as the pressure which drives it through is little or much above the healthy and normal pressure of the circulation. If the pressure be very slightly in excess, the material which transudes is a weaker solution of the salts of the blood with a trace of albumen; as the pressure increases, the proportion of albumen becomes larger; at length fibrin is found, perhaps only in flakes; a stage further, and it becomes sufficiently plentiful to impart to the transuded material the property of spontaneous coagulation; and finally the pressure may be such as to cause the rupture of the capillary vessels, and impart to the effusion a more or less considerable admixture of blood-corpuscles.

These various degrees are well illustrated in the pathological history of the kidney. If you have hyperæmia of that organ induced, either by interference with its escaping blood, or by too much impulse in that which goes to it, an increased exhalation occurs into the urinary tubules, and you get the symptom called albuminuria—one precisely analogous in its method of production to that of ordinary serous effusion in the cellular tissue of the body. If the disease advance, the Malpighian tufts pour out not only serum, but fibrin; and in this stage, if you examine the urine microscopically, you find this fibrin in the shape of little threads: these are accurate casts of the minute urinary tubules into which the fibrin was originally poured, and from which it often brings down, entangled in its substance, a certain quantity of the cell-growth of the tubule, the epithelium or

*endo*thelium. Finally, go a stage farther, and instead of seeing these little threads transparent, colourless, and of pure fibrin, you see a quantity of blood-corpuscles entangled in them; the capillaries of the Malpighian tufts have broken with the pressure, and have let all the elements of their blood escape; so that, instead of getting a mere fibrinous mould of the microscopical tubule, you get its little mould made of a thread of coagulated blood. These changes exactly illustrate the history of congestive and inflammatory effusion in all organs of the body; and as the kidney is peculiarly liable to such diseases—diseases, moreover, which are of the utmost interest and importance, you can hardly select a more convenient organ for exhibiting the changes in question.

And now, gentlemen, the inquiry that peculiarly belongs to our lecture of to-day is—what becomes of these inflammatory effusions when they are retained in the body? How do they terminate?

In approaching the consideration of this subject, remember, as the key for its right understanding, that the serous or fibrinous, or even bloody, effusion, of which I have spoken (if it occur from increased determination of blood to the part) is, in the strictest language of physiology, only an exaggeration of that ordinary nutritive supply, which conveys to the various organs of the body, and diffuses amidst their elements, the natural materials for growth. Remembering this, you will be prepared for knowing that all the true and immediate terminations of inflammation are processes of growth; accelerated processes, it is true, or perverted processes; but still processes essentially accordant with those by which the tissues were originally formed in the embryo, and are continually renovated in the adult.

Cell-development, formation of fibre, formation of vessels—these are the true and immediate terminations and tendencies of the inflammatory process; for the destruction of parts, in their molecules or masses, by softening and ulceration, or by gangrene—this occurs only incidentally in the process, only by indirect causation, and by the introduction of other influences than those which are essential to inflammation. To those primary and natural terminations I shall therefore at present confine myself.

The first changes which arise in an inflammatory effusion—changes often almost synchronous with the very act of effusion, are (1) the coagulation of its fibrin, and (2) the origination of cytoblasts.

1. Fibrin seems to coagulate in inflammatory effusions (just as in blood extravasated either within or without the body) by reason of its own specific physical qualities, and independently of any vital influence derived from surrounding parts. Indeed, I may go farther than this, and may say that the coagulation of fibrin occurs *in spite of* the influence of the surrounding living textures; for, just as effused blood will often remain for a long while uncoagulated within the body, while in contact with living parts, and while maintained at their temperature (as, for instance, in a serous cavity) and will soon become clotted when you let it flow forth into some dead receptacle;

just so will many inflammatory effusions refuse to coagulate while maintaining their original contact with an atmosphere of living parts, but will rapidly gelatinize, or at the least will precipitate flakes of fibrin, when artificially withdrawn from the body, and placed at rest in some foreign vessel. Even in so chronic an effusion as hydrocele, it is by no means infrequent to see transparent fibrinous clots form in a fluid which, at the moment of its traversing the canula, was perfectly free from such deposits. In short, the coagulation of fibrin is its *rigor mortis*, a change which essentially belongs to it as part of its process of death—a change which befalls it (1) when the whole bodily life ceases; or (2) when the blood in which it is contained dies prematurely and separately by withdrawal from the body; or, (3) under the circumstances now before us, when, either with or without the coloured elements of the blood, it is exuded or otherwise discharged from within the vessels, and is set stagnant and moribund amid the living textures of the body.

Under the microscope, you can commonly recognize coagulated fibrin by its clear, colourless, homogeneous, refractive substance; by its firmness and extreme elasticity; by the interspaces which are left in its mass, giving it the character of a network; and by a fallacious appearance of fibrous structure which is connected with its reticular coagulation. Sometimes you find the same material coagulated in small, separate flakes, which are perfectly structureless; and often you may see some such flakes as these lying unchanged amid the progressing products of inflammation.

You probably remember that, in speaking to you of the blood, I assigned some reasons for considering its fibrin an excrementitious product in the circulation, and consequently for hesitating to believe that it contributes to renovate the tissues of the body. I described to you its occasional increase in the blood, under circumstances apparently quite incompatible with its possessing the higher significance imputed to it by some writers; and I offered you an explanation of those endocardial valve-deposits which occur in rheumatic fever, to the effect that they might plausibly be considered as mere passive precipitations of fibrin, derived from a fluid overcharged with that product, and attaching themselves to a spot which offers mechanical facilities for their adhesion. These topics, relating to the natural offices of fibrin in the blood, are brought before us again to-day by our having to determine, what is the function fulfilled by it when it enters into true inflammatory effusions, and of what ulterior development does it become susceptible in its various abnormal relations.

On these points it is difficult to speak with certainty. Taking the fibrin separately, I should say that its tendency is to contract closer and closer together, with a vague appearance of striping, sometimes reticularly, sometimes with a disposition to tear in one direction rather than in another; but that this character is lost in the progress of contraction, and the nodule of pure fibrin becomes at length converted into a structureless granule of gristly firmness, which often becomes the seat of calcareous deposit. Such material

is often found in the peritoneum (where it is very wrongly confounded with the products of scrofula, under the name of tubercular peritonitis) and in a variety of other situations, besides forming those vegetations and thickenings, to which I have already adverted, in the interior of the vascular system. In this state, with very little change, small nodules of fibrin may be retained as permanent concretions; possessing, perhaps, just enough participation in the nourishment of the adjoining surface to maintain their half-vital existence.

Or, on the other hand, there may occur in fibrin the changes which I have already spoken of, as its softening and fatty degeneration: changes in which it becomes diffluent, presenting, under microscopical examination, an infinite number of the minutest granules, many of which are fatty, some, perhaps, proteinous. This is no doubt the final death and decay of fibrin; and it becomes matter of exceeding interest to know whether it be in this way that the fibrin of the blood naturally degenerates, previously to its elimination; and it is from their relation to this question that great interest is given to some recorded cases, in which a large proportion of fatty matter has been found in the blood, under circumstances which would rather have led the observer to anticipate an excess of fibrin.

It appears, then, that fibrin may remain stationary, and be nourished; or it may degenerate and decay: thus much is certain. But, may it advance? may it be developed into any higher form? into any tissue?

Notwithstanding the prevalence of a very general opinion to the contrary, I believe I may venture to question its possession of this power, and may say that I entertain extreme doubt whether, of itself, it ever shows the slightest disposition to cell-formation, or to any process of self-development.

Unfortunately, our opportunities of watching its solitary behaviour are very few; for, in almost every instance that can be thought of, albumen (which is probably the real regenerator of the tissues) is likewise present; and that great developmental activity, so often and so glowingly ascribed to fibrin, may, with at least equal probability, be considered the work of this associated albumen, for which (on this latter assumption) the fibrin could merely be considered to furnish an inert mechanical support. For think, gentlemen, if fibrin were that restless element of growth and vital expansion which some have fancied it, what a world of activity there would be in an aneurismal sac! A large aneurism, filled with laminated clot, has almost as much fibrin in it as the whole body put together; and yet it shows, on microscopical examination, no evidence of activity or of growth. At its circumference its pressure may have irritated surrounding parts, and may have provoked inflammatory effusion from them, but in the interior all is stationary and quiet. Towards the cavity, where the formation is most recent, lie the blood-corpuscles in a net-work of fibrin —the former in such numbers that the latter can but very imperfectly be seen; but in passing outwards, as the corpuscles seem more and more wasted, the fibrin begins to show more distinctly,

always adapting its meshes to the material within them, so that innumerable blood-cells are seen, each in its separate setting of fibrin: in getting still nearer to the circumference of the sac, the arrangement becomes confused, from the closer consolidation of the fibrin; but in no part of the structure have I been able to see any trace whatever of new organization.

There is a similar reluctance to the initiation of organic development in those other intra-vascular clots which form in tied arteries. They undergo changes referable to their blood-corpuscles, and they become pale and contracted; but their fibrin may remain for many weeks, or perhaps permanently, unaltered, except for some increase of density. I have seen it after the lapse of six weeks, showing only a vague appearance of longitudinal striation, with no essential change of physical character, and without the slightest trace of new development in its substance.

In an elaborate paper written by Dr. Zwicky on the metamorphosis of the arterial clot, a series of observations is given, which might appear to conflict with this opinion, but which, in reality, I think, confirm it. Where organization of the thrombus has occurred, he finds that it has been preceded by the following steps: first, there was the well-known clot with coloured corpuscles embedded in its reticular interstices; then gradually (while conglomerate bodies collected chiefly towards the apex of the clot, and while the coloured corpuscles diminished in number) the mass lost its appearance of striation, becoming amorphous and porous; together with this change, its base became very capable of infiltration from the blood-vessels about the seat of the ligature; next (a fortnight after the operation) it began to show cytoblasts; and from that time onward, as blood-vessels gradually became demonstrable in its substance, it proceeded to develop nucleated fibres at an increasing rate. Now the extreme tardiness with which the development of cytoblasts occurred in these cases, contrasts remarkably with their quickness of growth in inflammatory exudation; and for this reason it seems to depend on some new influence being imparted to the clot by the prolongation of blood-vessels into its substance (a process with which it is apparently simultaneous) much more than on any specific faculty of organic development residing in the fibrin itself.

I do not wish it to be understood as, in my opinion, a proved and certain thing, that fibrin is insusceptible of ulterior development; but I find, as yet, a want of sufficient evidence, to establish its possession of this power; and in the examination, both of intra-vascular clots and of inflammatory exudations, I find several facts which apparently militate against such a conclusion. In all such products, the fibrin has shown itself either stationary or retrogressive; either lying as first deposited, or contracting more and more densely; or altering, only to undergo degradation. So far as my knowledge extends of adhesive inflammation, and of the several reparative processes, I see no evidence that fibrin takes a more important part in them than that of holding the true albuminous blas-

tema within its meshes, and thus occasionally serving as a provisional matrix and scaffolding for the development of cells, fibres, and blood-vessels; and I cannot but suspect that those who have ascribed to fibrin so large a share in the processes of growth, have been somewhat under the influence of that prejudice to which I alluded in a former lecture, and have promoted this material to so high a rank in their pathology, merely because of its physical tendency to settle in a solid form.

Next, I have to speak of the formation of *cytoblasts;* and this is the real mystery, not only here in inflammatory products, but in every process of growth. A fluid, quite transparent, quite homogeneous, quite without visible forms in it, has sweated through the vessels: as soon as it is beyond the limitary membrane of the capillaries, there occurs in it a process, which (for the mere sake of having something to compare it with) one might speak of as an act of vital crystallization; the manifestation, namely, in a fluid menstruum, of definite solid living forms, deriving their properties from that menstruum in which they grow. But, if I have introduced the physical phrase, and for a moment have spoken of *crystallization*, it is only that I may the more strongly point out to you how eminently this process is *not one* having true analogy in any act of dead matter. Each cytoblast is a centre of growth—not as the microscopical crystal would be, by mere accretion to its surface, by mere sticking on of new particles: but of growth, by the interstitial appropriation of new matter, with the capability of self-development, according to definite types and laws, into shapes not included in the original pattern, and into purposes which are purposes of the system.

Each cytoblast, examined microscopically, is a little disc, sometimes quite round, at other times oval, or even a little irregular: when fully developed, it is about $\frac{1}{3000}$ in. in diameter, or larger, and is firm and solid in its substance. At earlier periods of its growth, it is seen much smaller, and of such delicacy that it requires care for its proper observation.

These little bodies are the germs of all future development; and, as respects the causes of their manifestation, all the information I can give you lies in a statement of the ultimate fact: Wherever fluid effusion occurs from the vessels, provided it be of a certain concentration, and maintained at a certain temperature, there these cytoblasts arise.

Two German observers (Lehmann and Messerschmidt) state that they have found these corpuscles manifest themselves within an hour from the infliction of an injury, and within four hours have seen complete pus-cells developed from them.

In speaking of the first appearance of these organic forms, I ought to inform you that the blastema in which they become manifest always contains a certain proportion of oily matter in the form of highly refractive globular granules, which run down the microscopical scale to the confines of invisibility. Many observers have believed that the cytoblasts arise in the cohesion of a certain number of these smaller particles, which have first developed themselves

independently; that the disc of the cytoblast is made by a certain number of elementary granules, placing themselves side by side. I do not know that this would at all simplify the matter, if it were ever so true; but, whether it would do so or not, I consider it, as fact, exceedingly doubtful. It has appeared to me rather the case (so far as I may trust my own observation) that the cytoblast is an organic unit from the first moment of its existence, not a patchwork of particles; that it grows very rapidly from an almost invisible size to the limit I have mentioned, and then commences the exercise of its peculiar functions. Some of those very minute oil-globules, however, do usually (or perhaps always) enter into the formation of the cytoblasts: and there is no physical improbability in the supposition that they may act as nucleolar points in the blastema, not indeed becoming confluent to form cytoblasts (since these are of a very different chemical constitution), but presenting a number of centres of aggregation, round which the proteinous growth may have a preference for showing itself. For some years it has been known by experiment, that such globules of oil, artificially diffused through an albuminous solution, will occasion the albumen to condense itself around them separately, enveloping each with a membranous film, as though it were a true microscopical cell.

The general statement of their origin, which I just now made, that, under certain conditions of *concentration* and *temperature*, they arise in every serous effusion, would seem to include an admission that they might develop themselves in the effused fluid, even after its withdrawal from the body. Such appears within certain limits to be possible; and though I can give you no observation of my own on the subject, I can quote one by Helbert (as given in Vogel's book.) He states that, having withdrawn the fluid from a vesicle raised by cantharides, and having satisfied himself by the microscope that it contained no corpuscles, he set it aside in a glass for five or six hours, and at the end of that time found in it exactly such corpuscles as are observed in wounds at the commencement of suppuration.

III. The ulterior progress of cytoblasts, in the inflammatory effusion, may be in either of two directions. On the one hand, you may see these little solid discs, remaining separate from one another, and continuing to float in the fluid blastema, grow and transform themselves into globular, nucleated cells, which form the characteristic corpuscles of *pus*. On the other hand, you may see their blastema condensing round them, forming a delicate inter-cellular medium, which at first is nearly or quite amorphous, but soon begins to show a tendency (and an increasing tendency) to split in one direction rather than another; and in the *fibrescent* blastema, which is thus constituted, you may see the original cytoblasts gradually prolong themselves, as nuclei, in the direction of the cleavage (perhaps determining that cleavage,) and receiving the accretion of new matter, partly at their sides, but chiefly at their opposite ends: so that, after a certain period of this axial development, they form

spindle-shaped bodies, which (like their blastema) show a disposition at their extremities to become fibrillated in one direction; and this is the formation of *new fibre.*

Mixed with the true inflammatory products, which I have mentioned to you, there often occur others, which are not essential to the process; and as these are particularly liable to strike you, in the examination of pus, it may be convenient that I should give you, specially, a short account of this fluid. In its normal state it is a smooth, greasy, viscid material, yellowish, of slight smell, alkaline, specific gravity averaging about 1030, and is seen microscopically to consist of a serum, with certain shaped products suspended therein. Of the latter, the essential and characteristic one is the so-called *pus-cell;* it is a globule, usually somewhat under $\frac{1}{2000}$ in. in diameter, pellucid, filled with some semi-fluid, albuminous compound, and usually containing, in addition, a few very minute oil-globules, which gave it a granular appearance. The addition of a drop of water to the preparation makes these characters plainer: the cell-wall becomes swelled out by the endosmosis of water, and the contained elements are rendered separate and distinct from each other. The cell has a nucleus, which, however, is not always visible without artificial means. Water usually makes it visible, as does very dilute acetic acid; and the latter reagent (when employed of greater strength) has the peculiar property of causing the nucleus to break asunder into two, three, or four particles. This test is considered diagnostic of the pus-cell.

These elements (serum, with cells of the properties just enumerated) are all that is necessary to constitute pus. The incidental elements observed in healthy pus are the following: (1.) Free oil-globules, usually of extreme minuteness, forming the granules which I have already spoken of in connection with the development of cytoblasts, and which are probably set free in the blastema very soon after its emergence from the blood-vessels; (2.) Free cytoblasts, undeveloped into cells, and various other immature stages of the pus-cell, in which the distinction of nucleus and cell-membrane just begins to be distinguishable; (3.) Compound cells, or glomeruli. This last form is a very peculiar and a very unintelligible one; it consists usually of a number of microscopical granules (such as I have already described) clustered into a globular heap, which may be almost three times as large as an ordinary pus-cell, and may either be invested with a cell-membrane, or may present the natural irregularities of its constituent parts uncovered and prominent, like the surface of a mulberry. The essential ingredient of these bodies is, as I have already mentioned, oily matter, and they vary considerably in their appearance, according to the fineness with which this matter is divided. The most characteristic are those in which the oil-drops are sufficiently large to be called *globules;* but these pass, by insensible gradations, to others (commonly called *granuliferous* bodies) in which the highest powers of the microscope are necessary to show that the finely-divided and almost impalpable contents are really of the same material as that which, in the *globu-*

liferous bodies, is more coarsely divided. I believe that in those where the contents are thus fine and granular, there is often a larger proportion of proteinous matter than in the others; but such differences are not abrupt; nor am I aware of any pathological inferences that can be drawn from them, as to the properties of the forms in which they occur. The forms in question are by no means confined to inflamed parts, nor even to parts ostensibly diseased. They are well known in the *colostrum* of the mammary secretion. I have seen them constituting almost the entire mass of an encephaloid testicle; and they are found in extreme quantity all about apoplectic effusions in the substance of the brain. In lungs which to all appearance are healthy, one constantly finds considerable numbers of such bodies; and here they shade off insensibly from extreme fulness and distension, to the simplest and most natural form of nucleated albuminiferous cell habitual to the parenchyma of that organ. In ovarian cysts they are likewise seen, varying extremely in size; evidently nucleated, where they are small; while, in the larger ones, the nuclei are apparently lost or hidden under an accumulation of granular contents, which here usually are in the minutest state of division, and often of a rusty or reddish colour.

With respect to the origin of these various oily *glomeruli*, it might easily be supposed that they had arisen in some extreme or irregular development of the normal pus-cell, or of any other nucleated cell peculiar to the tissue where they show themselves. On the supposition that their ripe condition is that in which they possess a cell-membrane, and have attained the largest size, it might be assumed that they were common nucleated cells, tending to hypertrophy by the ordinary method of growth, and filling themselves in their development with an inordinate quantity of oil; and it would be inferred that, having so filled themselves by some power of transformation exerted on the blastema around them, they subsequently undergo rupture, and suffer their previous contents to become effused among the surrounding tissue. Some curious observations, made chiefly by Professor Kölliker,* make it, however, very doubtful whether the real process may not be the exact reverse of this. He has seen blood-corpuscles included in the substance of these cells; and this would conclusively show, as he argues, that the cell-membrane is a subsequent formation in their progress of development. This view of their nature would imply that a number of the original oil-granules come into contact with each other, and cohere into a glomerulus, which subsequently becomes invested with a membrane, and constitutes a cell, the contents of which gradually undergo a retrograde development, and ultimately pass into the circulation. I cannot at present pronounce a decided opinion on this method of interpreting their history and phenomena. It would point, apparently, to their being organs for disintegrating and resolving certain elements of

* The first observation made in this matter was published conjointly by Kölliker and Hasse. It was strikingly free from the chances of fallacy, as to the identity of the blood-corpuscles, since it related to the morbid products of an animal in which these elements of the blood are oval.—Henle's und Pfeufer's Zeitschrift, vol. iv.

effused blood. I may admit, without hesitation, that they are peculiarly apt to present themselves where blood is undergoing re-absorbtion; you often find them in fibrinous clots of veins; Dr. Zwicky (as I told you) found them in the apex of the arterial clot; they have been found abundantly in retained catamenia; they are always present, I believe, where hemorrhage has been mixed with the inflammation; their granular contents (whether in large or in little globules) are such as constantly arise in the decay of fibrinous effusions; and the presence of blood-corpuscles in their interior could hardly admit of any other interpretation, than that they fulfil the functions suggested. Whether the original agglomeration of granules occur round a nucleus, or not, is a point on which no decided testimony is offered; but in organs where they are undergoing what Kölliker would consider their retrogression (*i. e.*, where several stages of transition are present, from the largest—destitute of a cell-membrane, and irregular as a mulberry on the surface, to the smallest—containing almost exclusively albuminous material, with only one or two oil-drops) in such organs, the smallest cells certainly present an unquestionable nucleus. Whether (on the assumption of Kölliker's theory) this nucleus was an original part of the glomerulus, or only developed itself subsequently to the formation of the cell-membrane, is a point on which I am unable to inform you.

While speaking of the peculiarities of pus, I ought to tell you that the suppurative process is modified, according as it occurs either on free surfaces or in solid organs. In the latter case, you have the formation of an *abscess:* that is to say, the inflammatory blastema is exuded in successive concentric spheres, the most central of which correspond to the first focus of inflammation, while the exterior thickness of deposit corresponds to a later date in the process. Thus it occurs, that the progress of suppuration gradually advances from within: here it is, that cells are first completed, that fibrin is first softened and transformed, that blastema is first fluid; and, on the same ground, the cyst of the abscess is intelligible as that part of the exudation-matter which has not yet undergone liquefaction, and which consists entirely of cytoblasts and incipient cells embedded in a network of coagulated fibrin.

The modification of the suppurative process which occurs in the inflammation of mucous surfaces is an interesting one. It consists substantially in this: that the suppuration gradually takes the place of the natural cell-growth of the part, without any destruction or alteration of its limitary membrane. It is essentially a process of secretion; a certain quantity of albumen, perhaps with some flakes of coagulated fibrin, first mixes itself with the natural secretion; then the latter gradually undergoes alteration; the characteristic epithelial cells of the surface drop in all stages of abortion, becoming first of all less squamous, and then gradually declining to small and simple albuminiferous cells; and with these are mingled many cytoblasts, apparently hurried from the surface before they have had time to undergo their legitimate development to cells.

It will be obvious, even from this sketch of what occurs, that the anatomical distinctions between pus and mucus must be as useless as the so-called chemical tests. Infinite gradations between the two fluids destroy all practical value in such alleged criteria. Mucus, as a copious fluid secretion, has no existence in health; the only natural secretion of a mucous membrane is its epithelium, which ought not to exist in quantity sufficient for any evident discharge. If the secretion be hurried, it immediately begins to assume the forms and physical characters of pus, even to the splitting of its nuclei by acetic acid; and most of the alleged distinctions then resolve themselves into this, that the pus of mucous surfaces usually contains little fat; it therefore does not so easily form soaps with the alkalies, nor produce the other chemical or optical effects due to the predominance of that material.

I have told you that the development of inflammatory products may take either of two directions—that into cells, with a fluid blastema, which constitutes the process of suppuration; that into fibres, with a solid blastema, which constitutes the process of adhesion. You would err, however, if you considered these processes to be quite incompatible with each other. In the adhesive process (as it occurs, for instance, in pleurisy) you never fail to find products which are quite undistinguishable from those of the suppurative process—complete nucleated bodies, presenting all the characters of pus-cells; and there can be no doubt that, in the majority of cases, these cells would afterwards undergo a retrograde development and decay, since it is quite certain that pus-cells, once formed, are insusceptible of ulterior true development. The phenomena of grannulation, too, consist essentially in a union of the two processes described; part of the exudation going, under the influence of new blood-vessels, to the formation of permanent tissue; while other cytoblasts advance a step further in the process of cell-growth, become possessed of a distinct cell-membrane, associate themselves with fluid blastema, and eventually drop as pus.

What determines the choice in each particular case, between the two final alternatives of inflammatory production—what occasions *this* part to form pus, and *that* part to thicken itself with new fibre, I cannot sufficiently tell. In comparing different tissues, with a view to resolve the question, there is extraordinary room for fallacy. Taking a general estimate of the phenomena, I should be inclined to view the difference as one essentially of *degree:* I should be disposed to say that the universal tendency of inflammation is to the suppurative process—that suppuration exists potentially in every inflammatory act. At one stage of inflammation the products are identical, and indifferent for either process; if at this stage certain conditions are withheld or withdrawn that are necessary for the completion of the inflammatory act, the blastema with its cytoblasts undergoes a fibrous development. What are those conditions? It would appear that the most considerable influence is that, which the inflamed tissue itself exercises on these its products. Thus, first of all, the degree of inflammatory excitement existing in the part influences the effusion

most importantly, and justifies us in considering the adhesive process an incomplete result of the inflammatory tendency; for constantly, by depressing the action of the part, we are able to preclude the threatened occurrence of suppuration; and with equal constancy, by giving additional excitement to tissues infiltrated with blastema, and likely to suppurate, we can insure their inflammatory products taking this latter course. Again, we find that suppuration is frequent where the inflammatory blastema is maintained in contact with the vessels which have produced it (as in the cellular tissue and in solid organs, where, most of all, the effusion is kept in the focus of the original excitement) and that it does not occur with equal readiness where these products are at once removed to a distance from the tissue which has evolved them, or are diffused over some large extent of membrane, where the influence of that inflamed tissue can be but little exerted on their mass. So too we find that (under equal amounts of excitement) a tissue, naturally active in its organic changes, is more likely to impress the suppurative tendency on its inflammatory products than a tissue naturally indolent—mucous, than serous membrane—gland, than periosteum. And this does not depend on mere difference of vascularity; there is no tissue in the body more vascular than the choroid of the eye, few which inflame more frequently, yet none which more seldom suppurates. It would seem that the cytoblasts of an inflammatory effusion assume activity in proportion to the organic excitement of the tissue in which they rise, and (according to the universal law of cell-growth) modify their own blastema by the exercise of a specific activity. When once they have undergone, even partially, the development into true cells, they become incapable of any other development; they may retrograde and decay, but they cannot advance except to suppurate.

It is curious, too, to observe how reluctantly they part from their characteristic influence over the fluid blastema in which they swim. In the surgical treatment of large chronic abscesses, it used often to be tried to obtain cure without discharging the matter, by promoting (as was then thought) the absorption of pus. Bleeding, or purging, or vomiting, or sweating, or other evacuations, were had recourse to, and not infrequently the fluctuating tumor vanished. But this was only for a time. A large proportion of the serum had been withdrawn from the contents of the abscess, and these had been reduced to little beyond cells; but, as soon as the blood had recovered its natural constitution, these cells (just like the nucleated cells of glands) again exerted their power, and surrounded themselves with their natural atmosphere. Accidental circumstances will often act like the treatment to which I have referred, and will reduce the fluidity of pus, so that an abscess apparently vanishes; but the cells may remain quiescent for an indefinite time, and may presently again surround themselves with fluid blastema, forming the same amount of pus as at first. The perfect and permanent absorption of an abscess—consisting not only in the removal of its serum, but in the destruction and dissolution of its corpuscles, so that the part shall

retain no tendency to the reaccumulation of its previous contents —this, I am persuaded, is among the very rarest occurrences in surgical practice.

If time allowed, I should be glad to point out to you how much light has been thrown on the pathology of inflammatory products, by that increased knowledge of structural anatomy, and especially of structural development, which the last few years have given us. The former doctrines of pus-formation were full of fancies; some theorists believing that pus arose in a direct conversion of the corpuscles of the blood; others, that it was formed by a deliquescence and solution of the sclid structures in its neighbourhood. It is chiefly to the researches of Schwann and Henle that we are indebted for that rational pathology of the inflammatory products, which enables us now to consider them in their affinity to healthy processes of growth, and permits us, in every stage of their development—from the first manifestation of cytoblasts to the ripening of pus-cells, or the completion of areolar tissue—to find in them an exact parallel to those natural processes which govern the progressive evolution of the embryonic tissues.

IV. Finally, with respect to the formation of bloodvessels amid the products of adhesive inflammation, a vast deal of uncertainty still prevails. You probably know that, in the earliest stages of the embryo, bloodvessels are developed with their contents as nucleated cells, ramifying from a centre in a stellate form, and sending forth long blind processes, which, meeting and becoming confluent with those of adjoining cells, constitute the first rudiments of arteries and veins.

It has been suspected, but never shown, that something like this might occur among the plastic efforts of inflammation. I will not venture to deny its possibility, but I have never seen anything which would justify me in speaking of it even as probable. What I have seen, and what I believe to be the ordinary arrangement, is this: the false membrane (for instance, a band of adhesion in the pericardium) will appear to the naked eye red and vascular; on submitting it to microscopical examination, you will see long lines of vessels running straightly from either side, to meet in the middle of the membrane, dividing, for the most part, dichotomously into parallel branches, and having very few anastomoses as they advance on either side; they are continuous with the vessels of their original surface, those of one side with the cardiac, those of the other side with the pericardiac vessels, and are evident prolongations of these respectively—but it is their peculiarity that they grow with great rapidity, and, at the time of their chief activity, are considerably larger than those vessels of the old tissue from which they originate. During their early periods of growth they show no transverse nuclei of contractile tissue, but they have abundant nuclei in their walls; and a very striking peculiarity, in the total arrangement of the structure, is the manner in which the nascent areolar tissue of the false membrane developes its spindle-shaped bodies along the lines of these vessels, adhering closely to their surface, strengthening their canals,

and following their ramifications, as a delicate nucleated sheath. Thus far, without question, the vascularity of the new tissue would appear substantially to depend on the prolongation of old vessels; and, on the whole, I think there can be little doubt that the process completes itself without any real origination of new vessels. Whatever difficulty there may be in this view, would relate to the establishment of anastomoses between those extreme branches which have run to meet each other from opposite sides of the false membrane. Their anastomosis is certain; and where they meet, there is often an irregular capillary plexus with large meshes. I suspect (though I am not sure) that these anastomoses likewise are made entirely by lateral offshoots from the prolongations of the original vessels: at least I have distinctly seen conical hollow processes, filled at their base with blood, advancing as though to meet similar processes from adjoining vessels on an intermediate area of false membrane, where certainly there has been no appearance of ramifying cell in the centre of the space: and as I have not at any other time seen any such cell among the products of inflammation, I am disposed to believe that these vascular prolongations ultimately coalesce with similar processes from the opposite and collateral capillaries, without the intermedium of any such new development from cells as that which occurs in the embryo.

LECTURE VII.

Tumours; description of them severally, as to their structure and usual sites: (1) Tegumentary;—cutaneous, mucous. (2) Vascular;—arterial, venous. (3) Fatty. (4) Fibrous; their calcification. (5) Cartilaginous; their methods of ossification. (6) Bony; simple, complicated with cancer; membraniform osteophyte of skull in pregnant women. (7) Encysted; follicular, vesicular, bursal, serous; contents of cysts; growths from wall of cysts; compound ovarian cysts; analysis of their anatomy.

Gentlemen: To-day I commence the subject of *Tumours*, and in my next lecture I hope to complete it—so far, at least, as I may venture to apply the word completion to this cursory treatment of a very important topic. I have thought it would be most convenient for you, that I should begin the subject altogether descriptively; telling you the chief characters of the several sorts of tumour, and showing you specimens of them; but reserving to the last all general reflections on their pathology, and all practical conclusions which may be deduced therefrom.

In starting, I will not even attempt an exact definition of the word; for until we have looked over the list of these products, you would hardly know what I might aim to include in, or exclude from, the precise phrases of any definition, however carefully constructed. Therefore, for the present, it may suffice to remember, that the word tumour, though derived from a learned language, may always be changed into a very familiar English synonym. A tumour means only a lump; and as we go on and proceed to examine those several lumps which are cut out, and put into bottles, and made preparations of, we shall gradually see that very dissimilar things are included under this one name, and that in consequence the title, even if sufficiently accurate for the purposes of practice, is somewhat inconvenient in pathology. Hereafter we may perhaps improve on it. To-day I shall speak of tumours under the following successive heads: (1) *Tegumentary*, (2) *Vascular*, (3) *Fatty*, (4) *Fibrous*, (5) *Cartilaginous*, (6) *Bony*, (7) *Cystic*, and (8) *Cancerous*, tumours.

I. Tumours arising in the *tegumentary* membranes of the body—in the skin and mucous membranes—and consisting of no other elements than those natural to the surface from which they grow, are common enough. In these cases, a portion of the skin or mucous membrane projects or hangs more or less beyond its level, and in growing may have more or less tendency to become pear-shaped, or to acquire a peduncle. These tumours are very common about the genital organs of the female—both outwardly, where they form pendulous masses, which hang from the nymphæ or clitoris, and inwardly, where they form polypi. The latter occupy, sometimes the vagina, sometimes the uterus; sometimes they have broadish bases, but more commonly very slender ones. In the examination

of such tumours you rarely find any other elements than those of the ordinary tegument, connected with some thinning of the cutis, and with some exaggeration of the natural areolar tissue. You generally find a loose and succulent stroma, which is infiltrated with serum, and consists of the meshes (perhaps widened) of the original areolar tissue. In the other and harder varieties, it would appear that new fibres are sometimes developed by the process lately described to you; in which manner these growths sometimes, but not often, approach to the structure and consistence of fibrous tumours.

The small, succulent, and pendulent tumours of the skin, which are known by the name of *molluscum*, answer to the above description. The immense pedunculated masses which are occasionally developed from the external genitals in hot climates, appear to be substantially of the same nature: such, for instance, is that in the Museum of Guy's Hospital, which the late Mr. Key undertook to remove from a Chinese, who was the subject of it. In the seventeenth volume of the *Medico-Chirurgical Transactions*, you will find the description of a similar tumour, which was removed, by Mr. Lawrence, from the pudenda of an English female. "Its tint was reddish gray; its structure was tough and fibrous, and consisted of condensed cellular tissue, entirely free from fat. It was left, during the night, on a large dish, and, in the morning, a very considerable quantity of fluid had escaped from it." That massive enlargement of the lower extremity, which occurs in *elephantiasis*, is probably of not quite the same origin as the above; but consists, to at least a considerable extent, of fibrinous œdema, and inflammatory thickening of the areolar tissue, and resembles, rather, that condition of the scrotum which, in hospital practice, we occasionally observe in persons who for many years have had the local irritation of urinary fistula.

It seems probable that many of the tumours called *sarcomatous*, though occasionally they occupy deep situations, are yet identical in nature with tegumentary tumours, and consist of no other elements than those of normal areolar tissue, sometimes with more or less new formation.*

In *warts* and *condylomata*, you do not see the same tendency to prolongation in the tissue; you find that there is an increased vascularity and prominence of the papillæ of the skin, and that these large papillæ support a vast increase in the ordinary quantity of epidermis. It is from their excess of epidermis, that warts, occurring in parts exposed to the air become horny; while condylomata or mucous tubercles, which are usually in moist places—in the axilla, or under the breast, or beside the mouth, or between the buttocks, or at the entrance of the vulva—acquire their characteristic flabby

* The so-called "common vascular sarcoma" is a mystery to me. In looking over bottled specimens bearing this inscription, I have seen pendulous tumours of the integument, fibrous tumours, fatty tumours, enlarged lymphatic glands, and various forms of cancer. When the name has appeared to be given with most precision, it has been assigned to some firm albuminous tumour, which consisted for the most part of cells tending to become elongated and spindle-shaped. I know no manner of distinguishing such a tumour from those extremely chronic cancerous growths, which by their large amount of fibrous transformation, evince an exhaustion of the diathesis in which they arose.

and spongy state. It is alleged that these tumours contain, and substantially consist of, a large quantity of new fibrous tissue, which gives support to the augmented epidermis, and assimilates their process of growth to that of granulation. In the few examinations I have had the opportunity of making, I have not found this to be the case.

II. *Vascular* tumours—tumours made up of bloodvessels—are very common in the skin, where they form the blue discolorations called *nævi*, which are so often congenital. They likewise occur in other textures, though far more rarely than in the skin. They are called by a variety of names, derived from their occasional or general characters—erectile tumours, aneurisms by anastomosis, or tele-angiectasies.

In their simplest form of cutaneous nævi, they may be described as adventitious cavernous structure. On a section, they exhibit the interlaced columnar appearance of ordinary erectile tissue—the columns consisting of fasciculated fibrous tissue, coated with delicate tesselated epithelium, which is continuous with that of the adjoining vessels; the hollow intercolumnar spaces communicate with one another, and are apparently the altered capillary channels of the part.

The mode of development of these tumours is unknown. It is Rokitansky's opinion that they arise as excavations in a blastema, which first of all is deposited in a solid form; and that the reticular structure thus established is eventually brought into communication with the original vessels of the part, by penetration of their walls; that it grafts itself upon them, and constitutes a diverticulum from the natural circulation of the blood. My own observations would hardly incline me to this view. In the large majority of cases, there is a total absence of any such solid blastema; in the history of ordinary erectile tumours, one finds no record of a period in which they had their bulk without their vascularity; nor, in their anatomical examination, do we find those stages of transition from a solid to a cribriform structure, or from a non-vascular to a vascular state, which Rokitansky's theory would lead us to expect. I see no reason for supposing that the development of vessels occurs, in the production of these tumours, otherwise than as I have seen it occur in the products of inflammation—otherwise, namely, than as a process of true growth in the original bloodvessels of the affected part.

In some very small proportion of instances, tumours of this kind are complicated by being made the seat of encephaloid growth; but here the coincidence is accidental, and the morbid anatomist has no great difficulty in deciding how much of the disease belongs to growth of bloodvessels, and how much to heterogeneous elements developed in their interstices. Erectile tumours commonly construct themselves in the skin; but sometimes they affect more important relations, involving bloodvessels of larger size. As they thus assume a greater importance to life, it is necessary to distinguish that they may be of two sorts; some have their chief relations with the veins, and the adjacent portion of the capillary system; others rather with the arteries and that portion of the capillaries nearest to them.

The latter (which of course pulsate) have frequently been developed in the interior of bones; where they simulate (if indeed it can be called simulating) the character of ordinary aneurism. You will find several interesting cases of this sort detailed in Mr. South's translation of Chelius's Surgery. The other variety, which chiefly affects the venous half of the circulation of a part, has some affinity to varicose tumours. You will find a very good illustration of this form in a case reported in the thirtieth volume of the *Medico-Chirurgical Transactions*, by Mr. Image, surgeon to the Suffolk General Hospital. The left breast was enlarged by an erectile tumour. It was pendulous, and of a bluish or a slate colour, with some darker patches in the vicinity of the nipple. It did not pulsate. Round the base it measured twenty-three inches, and thirteen across. Compression, so as to empty it, produced a feeling of internal plethora; while conversely, allowing it to refill, caused faintness. The patient died twenty-two hours after the operation of tying it, in which he had lost fifty ounces of blood. The internal mammary vein had, towards the subclavian, a sacculated appearance; between each sacculated portion and the heart the vein was narrowed and thickened; the sacculated parts were formed of one hollow within another. The mammary veins, external and internal, were traceable into a cellulated structure, of which the whole tumour consisted—it being, in fact, a collection of cells formed of the venous branches.

In health, the elements of the fibrous structure of the organ are parallel, and closely united; here they had given way to the dilated veins. Their texture was entirely altered, being converted in some places into a kind of network, through which the vein-cells passed.

III. *Fatty* tumours. These, whether examined by the naked eye, or with the assistance of a microscope, show only elements which perfectly accord with those of normal fatty tissue—viz., cells, which are from 150th to the 300th of an inch in diameter, with a definite cell wall, and sometimes, but rarely, a nucleus, and which contain fat in their interior. Chemically, this fat is identical with that of the normal adipose tissue, consisting of elain and margarin. Sometimes the latter is present in so large a proportion that, as the texture cools after death or extirpation, it separates from the elain, and solidifies in peculiar stellated groups of acicular crystals in the interior of the cell. All the fat of such tumours is naturally contained in the cell membrane: free oil-globules only exist where cells have been ruptured.

The firmness of fatty tumours varies, partly according to their chemical constitution, and partly according to the development of fibrous tissue in them. Sometimes this tissue will abound in them, forming numerous partitions between parcels of fatty cells; sometimes, on the contrary, there will be very little of it.

As respects situation, these tumours may arise in most parts of the body; but in an infinite majority of cases they occur in the subcutaneous areolar tissue. Sometimes they have a deeper origin. Two years ago I removed one, at this hospital, from a periosteal at-

tachment to the humerus, where it lay under cover of the brachialis anticus muscle; and some years ago, at King's College Hospital, I removed one from beneath the infra-spinatus, where it lay in immediate contact with the surface of the scapula. Occasionally, they arise still more deeply, in connection with the mucous, serous, and synovial membranes; but these cases are rare.

Fatty tumours have a capsule of slightly condensed areolar tissue, through which they receive their vessels. They are but loosely attached to it, so that, in operations, they are usually turned out with facility. The capsule hardly ever bleeds sufficiently to require a ligature; but very often (if pressure be not made) sufficiently to fill itself with clot, and to cause subsequent inconvenience.

Their growth is slow, and almost unlimited; their indolent progress, together with their lobulated form, and soft doughy feel, usually establishing their diagnosis.

IV. *Fibrous* tumours, such as you often see under the peritoneal coat of the uterus, are apparently a well-marked division; distinguished by their demarcation, which causes them to look as if they had been stuffed into organs, and could be turned out of them. They cut something like the intervertebral disk, or that of the symphysis pubis; and show a grayish, glistening surface, with manifest white bands, which are intimately interwoven, and take a curvilinear and often concentric direction. This character is peculiar, and helps to mark them. They have singularly little vascularity, especially when the concentric arrangement is most distinct. When examined by the microscope, their fibres show the general characters of normal fibrous tissue, but are less undulating. In the intervals between the fibres we frequently find cells, sometimes stationary, sometimes undergoing development into new fibre, and on the older fibres we often find traces of the original nuclei.

Sometimes the fibrous growth appears to have commenced simultaneously at several centres, so that its mass is lobulated, or perhaps may rather be said to consist of a plurality of smaller fibrous tumours, with an intermediate tissue which is more lax and vascular. It is particularly in masses of this sort, and apparently in the looser intermediate tissue just referred to, that a quantity of serous fluid is occasionally found, simulating the characters of a true encysted collection. In some organs (as especially in the ovary, the breast, and the testicle) fibrous growths often concur with another alteration, which leads to the formation of true cysts, constituting the so-called fibro-cystic tumour of these organs.

It is a peculiarity of these tumours that they consist entirely of gelatinous material; the very faint trace of protein discovered in their larger masses being due, no doubt, to some quantity of retained blood. Their growth is very indolent, and the transformation to which they are most liable is that of *calcification*, wrongly called ossification—a process, namely, in which no true bone is formed, but earthy particles are deposited and accumulated in the organic basis of the tumour, so as to make a mass which is sometimes friable and porous, sometimes hard and dense as marble. Another

change which they sometimes undergo, and one to which they are all the more liable for this previous calcification, is the process of expulsion from the system. This has occasionally occurred with those attached to the uterus, especially if seated under its mucous membrane; for in these cases, when the organic connections of the mass have gradually been loosened in the progress of its degeneration, the expulsive power of the uterus leads to its removal, either entire or in pieces.

They are observed in very various relations—in connection sometimes with bones, sometimes with glands, sometimes with mucous or serous membranes, or rather with their subjacent tissue. Their favourite seats, however, are the uterus and ovary, the dura mater, and the mamma. More than one are sometimes found in any organ which they affect, but it is rare to see them in several organs.

Fibrous tumours are likewise liable to various atrophic processes, which lead to their softening, a change which commences in their interior, and leads to the formation of a central pseudo-cyst, containing *débris*. These processes may produce necrosis and decay of the whole mass.

V. *Cartilaginous* tumours, or enchondromata, almost always affect the bones. Of thirty-six cases given by Mueller, there were thirty-two in the bones, (viz., twenty-five in the metacarpus and phalanges, three in the tibia, one in the ilium, one in the cranium, and one in the ribs,) one in the parotid, two in the testicle, and one in the mamma of a dog.

Sometimes they arise from the exterior of a bone (perhaps from its periosteum) sometimes from its interior. In the latter case they expand the cortex, and, as it gradually thins, spread it out into a globular sac, or make their way through it by perforation. They grow slowly and with little pain. When uncut, they appear as rounded masses, often lobulated, seldom very large, encased either in new fibrous tissue, or perhaps in distended periosteum, or in an expanded cortex of bone. On a section, they show a surface which, to the naked eye, often appears uniform; it is compact, bluish-white, semi-transparent, and glistening, like that of the fœtal skeleton; and under the microscope presents characters which are identical with those of true cartilage—namely, nucleated cells, set in a firm, pellucid blastema, which is sometimes quite homogeneous, and sometimes, like the cartilage of the ribs, shows a disposition to split in fibres. The elementary cells of these tumours often contain two or three nuclei, or as many young cells in their interior. The sensible characters of cartilage immediately depend much more on the blastema, or inter-cellular substance than on the cells themselves; and in the examination of enchondromata, as well of the natural cartilages, we find differences as to the degree and extent of cell-development, so that they are sometimes little advanced beyond their nuclear condition; sometimes, on the other hand, nearly as large and as active as in the ossifying epiphyses of the fœtus.

The sectional surface of a cartilaginous tumour will often be otherwise than uniform. Sometimes it will be intersected and lobulated

by strong fibrous bands, and will appear to be composed of numerous rounded masses, severally invested and united together by these fibrous processes of the general capsule. Sometimes their uniformity will be broken either by softening or by ossification. In the former case, the tumour will present various loculi, with firm walls and gelatinous contents, which suggest a similarity to some forms of colloid carcinoma, or it may have a single large excavation in its interior.

Ossification is the natural tendency of cartilaginous tumours, and is a result which, in some part or other of their substance, they generally attain. It differs from the so-called ossifications of fibrous tumours and of arteries, in so far that the structure formed is one of true bone, presenting the natural vascular canals and lacunæ of osseous tissue, though commonly without so definitely laminated and concentric an arrangement as that which we find in the normal skeleton. It more nearly resembles that irregular solidification which pervades the cartilages of the larynx, or of the ribs, when they ossify. It may occur in either of two forms; sometimes the process will advance (if I may use the phrase) in a single *wave* of ossification, from the attached to the distal part of the enchondroma, keeping just behind the new growth of cartilage; so that, in the case of a pedunculated exostosis, the tumour will appear ossified everywhere but at its most prominent parts. Sometimes, on the other hand, numerous independent centres of ossification will arise in the cartilaginous mass, and, at an early stage of the change, will show themselves, on microscopical examination of the translucent substance of the cartilage, as an infinite number of star-shaped crystalloid opacities, which radiate their acicular fibres in all directions. These separate centres would presently become confluent.

VI. *Bony tumours* (if distinguished, as they ought to be, from mere calcareous concretions) very rarely occur except in immediate connection with the normal skeleton. In most instances they present themselves as a sequel or a complication of other morbid growths. Thus we have already seen that they are apt to constitute the natural termination of enchondromatous tumours, and to complete the development of their structure, according to the general process of cartilaginous ossification. Probably all tumours which consist of true osseous tissue, even if they have not demonstrably been preceded by the growth of actual enchondroma, have at least had a limited formation of cartilage-cells in immediate priority to their development of bone. When soft cancerous tumours are developed from the periosteum, or are otherwise in immediate relations with bone, it is very frequent to see the morbid mass furnished with an adventitious skeleton, by the prolongation into its substance of long stalactites of new bone, which take their origin from the old one, and which, in their union with the softer material of the encephaloid disease, have the name of *osteo-sarcoma*. Our museum contains instructive specimens of bony tumour under both these heads; somewhere the new bone presents itself as the advancing ossification of an enchondroma; others, where it has shot forth in long foliaceous processes from the shaft

of a normal bone into the pulp of an adjoining encephaloma. In both these classes of disease, the osteophyte presents the microscopical characters of true bone; and Mr. Adams has shown me a specimen of what is supposed to be far less common—the presence of these microscopical characters in a bony mass developed in the substance of a fungoid tumour *not* attached to bone.

A considerable number of so-called osteophytes are membraniform in their arrangement; they consist, for the most part, in the solidification of inflammatory effusions, by a process similar to that which determines the ossification of callus. Such are common nodes; such, too, are many of the growths of new osseous tissue which accompany chronic disease in the shafts of the skeleton. This is not the most suitable time for speaking of them; but I may avail myself of the opportunity to mention to you one very remarkable kind of membraniform osteophyte, which Professor Rokitansky discovered to be an usual and recurrent phenomenon in connection with the state of pregnancy. He found that, within the *calvaria* of a considerable proportion of puerperal women examined by him at Vienna, there lay a fine lace-like deposit of porous new bone, adherent to, and identified with, the inner table; that this deposit, where very plentiful, was sometimes distributed more or less over the whole vault of the inner table, and also showed itself in patches at the base; but that it occurred with a marked preference on the inner surfaces of the frontal and parietal bones, especially along the longitudinal sinus, and most of all on those mammillations of the surface which separate the convolutionary impressions of the brain. The earlier stages of this delicate osteophyte consist in simple exudation, followed by the formation of cartilage—a process identical with that of node-formation in periostitis. Each new pregnancy tends to add another lamina to this growth, and where several such layers have been formed, they are preserved (at least for a long time) distinct from each other by a sort of diploe, which intervenes between them; so that their aggregate might furnish a sort of tally of the woman's puerperal achievements, as the rings of wood in a tree indicate the age of its trunk. The specimen in our museum, which illustrates many of the points to which I have adverted, was kindly given to me by Professor Rokitansky, from whom also all my information on the subject is derived.

VII. *Encysted* tumours.—This is a very common name, and may therefore serve to head a class of tumours; but it is rather an objectionable one; for the word "encysted" means, inclosed in a cyst; hence the tumours in question are not, strictly speaking, *en*-cysted, but are themselves cysts containing something. They are tumours, in which you can distinguish and separate cyst and contents; but in which both cyst and contents equally go to make up the tumour.

1. Cysts very commonly occur about the scalp, face, lips, eyelids, and urethra, and are frequent subjects of surgical operation. In addition to their own proper substance, they are frequently surrounded by a quantity of condensed areolar tissue. In the lip and eyelid, their contents are often glairy; but those of the scalp contain a peculiar

cheesy stuff, which may be smeared out like pomatum. On microscopical examination, this material is found to consist entirely of nucleated cells (which are shrunk and reduced to the character of scales) mixed with a good deal of free oil, occasionally with plates of cholesterine, and sometimes (as Mr. Gulliver has shown) they contain a granular calcifying deposit of the phosphate and carbonate of lime; sometimes hair is found in them. These contents are just such as are found in the neighbouring follicles of the skin or mucous membrane; and it is quite certain that the tumours in question consist of nothing more or less than these follicles dilated. From some cause or other an orifice becomes obstructed, and the contents of the follicle accumulate and distend it to almost an indefinite extent. Meanwhile, its outside is thickened by new areolar tissue, and is thus supported under the extreme distension to which it is subjected.

But sometimes it gives way, and then one of two things may occur: Acute inflammation may be excited in and about the sac, suppuration may ensue, and ultimately the disease may be cured by a granulating process; or, more rarely, the burst follicle may continue to secrete, and the mass, drying as it grows from the cavity, at first looks like a rupial crust, but presently becoming longer and longer, it forms an actual horn on the head, and requires removal, partly because of its real inconvenience, and partly because of the mock pity which is awarded in society to the wearer of such an appendage, who gets, at length, like the inhabitants of the Island of Minorca, "never to mention it but in anger, and then to curse with it, saying *cuerno*, as he would *diablo*." There is a very ready transition from these tumours to that cyst called ranula, which appears under the tongue, from obstruction of the sub-maxillary duct, and which consists of that duct in a dilated state, full of saliva more or less changed.

Many authors believe that cysts in the breast, testicle, and kidney, are to be accounted for in a similar way; but so far as the latter organ is concerned, I seldom pass a week without seeing appearances which cannot be accounted for on this mechanical supposition; and I feel difficulty in admitting its correctness as a general rule with respect to the other organs. Many, though perhaps not all, of the simple cysts which arise in the ovary, and (I believe) all those which are developed in the thyroid, are formed by the distension of normal cavities. This distension depends on an excess of secretion into cavities which are naturally closed. The contents consist of the ordinary product of the gland, often with little change beyond some exaggeration of its ordinary development; and the disease may consequently be considered a simple act of "secretional hypertrophy."

But it seems incontrovertible that cysts may arise separately from any secreting structure. I had an instance here, some time ago, in the post-mortem examination of one of my female patients, where a simple serous cavity had been formed between the peritoneal and muscular coats of the intestine. About the same time, in one

of the lower animals, I found a similar bursal cavity, of considerable extent, and with polished walls, without any apparent destruction of tissue, between the muscular and mucous membranes of the stomach. Five or six years ago, I had a case of large cystic tumour, developed out of contact with any secreting surface—unless, indeed, it were with the lymphatic system; it lay deeply in the neck, under the sterno-mastoid muscle. Two or three months ago, I opened a similar cyst, situated in a gentleman's perineum, just beside the tuberosity of the ischium. They are not infrequent in connection with the jaws; thus I lately opened one situated in front of the malar process of a young woman.

Where cysts arise, as in these instances, separately from natural ducts or follicles, which might give birth to them, their mode of origin is commonly at the expense of the areolar tissue. The simplest illustrations of this formation are to be gathered from the history of subcutaneous synovial bursæ, many (if not all) of which are formed subsequently to birth. Pressure, with friction, exercised upon some movable part of the integument, gradually causes a rarefaction of the areolar tissue beneath; its meshes become large, and infiltrated with fluid; presently a certain space of it becomes marked off, and environed by an increased growth of areolar tissue at its circumference; a cavity is thus formed, from which any remaining pillars or septa of areolar tissue gradually vanish, and its interior becomes polished, acquires an imperfect epithelium, and fulfils the duty of a synovial cavity. You see this process at work on the olecranon, and over the tuberosity of the tibia; and especially, in persons who suffer with *talipes internus*, you constantly see large bursæ developed on the dorsum of the foot, which is, in them, preternaturally exposed to friction.

The actions by which these cysts are constituted may run to excess, if the circumstances calling for their existence are of immoderate operation. Such excessive results may be in either of two directions. On the one hand, the fluid secretion may be excessive, leading to a bursal dropsy; and this augmented effusion (like all stimulated secretions) may tend to become more and more albuminous, and the lining membrane may readily pass from this over-active condition into a state of true inflammation, accompanied by its ordinary products. Or, on the other hand, the limiting process of fibre-formation may become redundant, and successive layers of fibrous growth may accumulate at the circumference of the cyst, gradually converting into a solid, knotty tumour, what was designed for a synovial cavity. It is particularly over the *ligamentum patellæ*, that the bursa becomes liable to this fibrous transformation, and it has happened to me three times within the last year, to be obliged to remove tumours which had arisen in the manner I have described to you.

I might occupy an entire lecture (though very unprofitably) in describing to you the various contents which are found in simple cysts. Of the follicular, I have already spoken. The bursal contain synovia, which chiefly varies in respect of the inflammatory ad-

ditions just alluded to. Those cysts which arise without any obvious cause often contain blood; and mixed with this will be other cell-forms, representing the epithelium of the cavity, and very generally a considerable proportion of those compound granuliferous cells described in a former lecture. Simple ovarian cysts contain an albuminous fluid, with an abundance of cell-forms, rich in oil; they likewise constantly contain plates of cholesterine, and blood-globules are not very unusual; their granular cells reach a much larger size than any I have observed, and contain the material, whatever it may be, that determines the colour of the total fluid. Some years ago, in examining a specimen of very dark fluid from an ovarian dropsy, I found that the large granular cells were the seat of this colour, and I likewise found that the fluid contained a very large proportion of iron. These ovarian cysts have at times been found to contain materials like those of the cutaneous follicular tumours. And Mr. Paget has pointed out the interesting fact that, in such cases, a part of the cyst-wall has, from some cause or other, acquired the structure of true skin; that it has a cuticular surface, hair-follicles, sebaceous and sometimes perspiratory glands; and he infers that "the structures and secretions formed on this portion of the cyst are shed into its cavity, and there accumulate, and they remain when, as often happens, the cutaneous structure on which they were produced has degenerated and disappeared."

A very remarkable variety of cysts is distinguished by the peculiarity of having solid vascular growths developed from its walls; but though this peculiarity is very striking, yet the cysts so occupied by solid growth are found quite undistinguishable in their remaining characters from other cysts contained in the same organ, and destitute of such vegetations. This intra-cystic growth will occasionally be seen in specimens of encephaloid disease, as fungoid masses projecting into serous cavities, and tending to fill and obliterate them.

But especially this is the case in that disease of the female breast to which Sir B. Brodie has given the name of *serocystic sarcoma*, and of which you will read the most perfect description in his lectures. Its peculiarity consists in the production from the cyst-wall of cauliflower-like growths; which, as they advance, gradually encroach on the cavity of the cyst, obliterate it, coalesce with its walls, form a solid tumour, and eventually may undergo still further evolution; traversing the skin, and fungating through the aperture they have caused. Similar excrescences may apparently likewise grow from the exterior of the cysts. In structure, these growths are lobulated, looking on the surface like a mass of warty granulations. On dissection of the separate lobules, they break into minute dense leaflets; any one of these, examined by the microscope, shows a very definite limitary line, within which a fibrous tissue is perceptible. This tissue, while in the structure of the leaflet, shows some appearance of a definite striation, diverging obliquely from the axis; when torn asunder, it displays distinct separate fibres, something like those of elastic tissues; but in the specimens which I have examined, it presents no traces of cell-growth. Why cysts in the

mammary gland should have this peculiar tendency to develop fibrous vegetations, is a difficulty on which I can offer you no information; but, as regards the anatomy of the disease, I believe that I have given you the leading features; that it is essentially fibro-cystic; that it consists in the formation of simple cysts, complicated only by the growth of fibrous tissue, which is compacted or ensheathed in the form of branching leafy processes.

Here is the place to mention those *compound cysts* of the ovary, to the peculiar anatomy of which Dr. Hodgkin first drew attention, as consisting, according to him, in a tendency to develop new cysts from their wall; which new cysts, growing inwards with the elder cyst-membrane folded over them (just as the pericardium is reflected over the heart) gradually fill and obliterate the original cavity. They then, in their turn, become liable to the same parental office, and give origin to a tertiary race of cysts which grow from their serous interior, and presently fill their cavities, acting by them as they acted by the primary cyst. He mentions it as characteristic of this method of growth, that the branches or clusters of secondary cysts are invariably and permanently attached to and continuous with the internal surface of the elder cysts in which they are contained; which attachments may be by broad bases or by narrow peduncles.

The anatomy of these compound ovarian cysts, so accurately described by Dr. Hodgkin, and illustrated by specimens which abound in every pathological museum, is hitherto quite inexplicable. The description which I have given of sero-cystic disease in the breast will justify me in regarding that affection as utterly unlike the one now under our notice—utterly unlike at least in all essential particulars; and I have therefore refrained from considering them together. Confining myself now to the ovarian disease, I would tell you that its essential phenomenon may be described as a cyst-growth, *tending to become perpetual by means of the endogenesis of a new cyst similarly prolific.* This phenomenon stands, I apprehend, quite alone in the economy; it constitutes a disease essentially self-reproductive—a disease in which each step tends to provide for the succession of another similar step; and in this respect it bears much nearer analogy to the increase of parasitic organisms than to the progress of any known structural disease. And as I reflect on the organ in which alone this mysterious disease occurs—an organ as special in its function as the disease is special in its nature; as I find that it is only in that germ-bearing organ that this germinating disease is known, and that it constitutes there a morbid mimicry of the reproductive function;—I cannot but connect these facts together as a clue to interpreting the disease; a clue which, to my mind, I confess, strongly suggests the possibility of an unimpregnated ovum spontaneously undergoing these acts of pseudo-development, so as to simulate the relations of a parasite towards the organism in which it occurs.

LECTURE VIII.

Tumours (continued): Cancer; type illustrated in encephaloma of the eye; its anatomical ingredients; scirrhus; colloid; usual sites of cancer; distinction of primary and secondary; modes of dissemination;—by contact; by veins; by lymphatics. Can it be infected by inoculation or injection? PATHOLOGICAL RECAPITULATION: (1) Tumours by accumulated secretion. (2) Hypertrophic tumours; partial hypertrophy; adjunctive hypertrophy. (3) Hypertrophic tumours with conversion of tissue. (4) Eliminative tumours. What is the malignity of cancer? operations for its removal; the pathological principle on which their occasional admissibility rests.

GENTLEMEN: Resuming the consideration of tumours at the point where I broke it off at the close of my last lecture, I now proceed to speak to you of Cancer.

Under this generic name are included several varieties of disease; differing from one another in many sensible details of colour, consistence, shape, rate of increase, and the like; but agreeing with one another so truly in all essential particulars relative to the laws of their manifestation, as to establish a fundamental similitude between them, and justify the pathologist in accounting them a single family of morbid products.

In Rokitansky's incomparable work (now translating under the auspices of the Sydenham Society), and in the monographs of Dr. Walshe and Dr. Bennett (the latter very copiously illustrated with accurate illustrative wood-cuts), you will find the differential characters of the several species and varieties of cancer treated in full. For me, in a single lecture, it would be impossible to do more than impress on your minds the larger outlines of the subject; and to that endeavour I shall the more willingly confine myself, as I am persuaded that all useful and practical knowledge of the disease must be discoverable, rather in those bold features which are common to its several forms, than in the minuter distinctions which individualize a specimen, or constitute a variety.

Taking, then, out of innumerable instances that which, to my mind, seems most characteristic and typical, I would sketch you an illustration of cancer thus: A child is brought to me, blind of one eye. The loss of sight has been discovered accidentally, for there had been no complaint of pain. The pupil is largely dilated, but (with this exception) at first the eye looks healthy; the iris having its natural colour, the cornea its natural clearness and polish, the globe its natural mobility. On looking carefully, however, through the large dark pupil into the depths of the eye, I observe there (as the patient's head moves) an unusual reflection of light, as though from a small metallic mirror set in the retina. A month elapses, and I see the child again: the aspect of the large dark pupil is now altered by something white or yellowish, which seems to stand close

behind it, rising from the bottom of the globe—something solid, smooth, rounded, reflective, with a red vessel or two branching on its surface. Another interval of longer duration, and I find what can no longer be overlooked, even by the non-professional observer: that pale, growing mass has advanced into the anterior chamber; the lens has become opaque, and is thrust aside, or merged in the tumour; the globe is no longer healthy in appearance, but is enlarged in its transverse diameters, and seems to bulge unevenly at one or two points of its circumference; evidently it is distended, and its distension causes pain and irritation; the vessels of the conjunctiva are gorged with blood. A few weeks more—the cornea has sloughed before the augmented pressure of the tumour; the latter has burst from its confinement, and though still girt about its base by the ring of sclerotic, it expands beyond this isthmus with redoubled luxuriance, into a mushroom shape, with broad, bloody, discharging surface. Now every day tells: the sclerotic ceases to constrain the expansion of its base, which no longer seems to emanate from the globe merely, but from the whole cavity of the orbit; while its outward growth has thrust the eyelids wide asunder, and projects already far beyond their level; its discharge is immense; lumps slough from its surface; blood bursts from its vessels; a material like pus pours from it incessantly; but in spite of all this loss of substance it grows on, bigger and bigger; the wretched child meanwhile getting thinner and more hectic, as though its whole organic subsistence were gradually prolapsing through the orbit. The surrounding integuments have taken on the same fungoid activity: where they correspond to the base of the tumour, they no longer seem to confine, but rather to contribute to, its growth; blending their large pulpy vegetations with its broadened circumference. One marvels whence can be derived its flood of albuminous secretion; one hopes it may exhaust itself, and cease like the flux of an abscess; but such hope is vain: the duration of life and the circulation of blood are the only limits of its continuance.

A little while longer gives the opportunity of *post-mortem* examination. The orbit is tightly occupied with what may still be called the base of the tumour—so tightly, that, if the case have lasted long, the bony walls of the cavity will have begun to undergo absorption. A section of the tumour shows a substance like brain, white, soft, and uniform, which admits of being cut in thin slices, but may easily be rubbed to a cream. It is marked with red points, indicating the section of bloodvessels, and in parts is pinkish over the surface, from diffused vascularity. It is intersected and supported by a very delicate network of fibrous tissue; from the interstices of which there may be squeezed or washed out the softer pulpy elements of its structure; leaving only that slight alveolar web, as its skeleton, behind. Microscopical examination shows that this mass consists substantially of nucleated cells, presenting some varieties of form, and some gradations of development, to which I shall directly give closer attention.

On opening the cranium, it is found that the same morbid change

has prolonged itself thither: the optic nerve immediately within its foramen enlarges into a lobulated mass of material, like that of the exterior disease, which extends as far as the thalamus, becoming larger behind the commissure of the optic nerves, and indenting the adjacent surfaces of brain, which are in a softened and diffluent condition from the effects of pressure.

This picture of encephaloid cancer, as it affects the globe of the eye, is one that many of you can verify out of your own recollection; and all of you no doubt can remember some case where the family-likeness of cancer showed itself in one part of the body or another; —some case, in which a solid tumour has made its way through the skin, has continued to grow and shed its particles outwardly, has shot its roots further inward, has infected all parts around with its peculiar method of growth, and finally (supposing it to have resided in no vital organ) has destroyed the patient by sheer exhaustion and flux.

Keep such a case as this in your thoughts, while we argue about cancer; for it is in such that the natural history of the disease receives its best illustration.

Now, what are the anatomical elements of such a tumour as I have described, or rather of encephaloid tumours in general? Essentially (as I have said) forms and steps of microscopical cell-growth: round or oval cells, like pus-globules, with dotty contents, and with a nucleus more or less distinct; or cells, like those of glands or ganglia, more opaque with granular material, round or angular, or developed into processes, and having one nucleus or several; or gigantic mother-cells containing within them simple cells of a new formation, or nuclei and granular matter; or cells in various degrees of blackness with pigment, perhaps to an amount which shall render the whole mass *melanotic;* or spindle-shaped bodies with oval nuclei, indicating the commencement of new fibre; or free nuclei—some round and oval, with single nucleoli, having the size of normal gland cytoblasts, others twice or thrice as large, elliptical, with double nucleoli; or elementary granules of all sizes, or glomeruli consisting of them. And, for the intercellular material—it has no high development in such cases: sometimes it will be so amorphous and incoherent, that the microscope cannot identify it; sometimes it will be more fixed, but scarcely more shaped, having the faintest appearance of fibre, and carrying a few elongated nuclei in its substance; sometimes in this form it will be more distinctly membranous, opaque, and fibrillated; sometimes spindle-shaped bodies with nuclei will be arranged as septa; sometimes there will be a developed fibrous framework, forming distinct alveoli for the cellular elements of the tumour; sometimes, though very rarely, there will be a bony stroma for the growth, supporting it, not at its base in the form of an osteophyte (as when in contact with normal bone) but actually spread throughout the tumour, as a fine diploe, within which the cancerous germs lie as marrow.*

* Rokitansky, vol. i. p. 368.

To complete this statement, I should add, that the products of hemorrhage in greater or smaller quantities will often be found in these tumours, constituting the variety of *fungus hæmatodes:* that large granuliferous cells, with more or less abundance of free oil, will be seen in them, often gathered in clusters, which to the naked eye seem yellow; often diffused in lines which run together in plexuses, and constitute an appearance, which Mueller believed to be characteristic of one species of cancer (hence named *reticulatum*) but which belongs to all at one period of their development; and finally, cysts will sometimes be noticed in combination with these encephaloid elements, and may or may not have their cavities partially occupied by the further growth of such elements in their interior: the latter possibility being chiefly illustrated in the breast, brain, and testicle.

The chemical constitution of encephaloid cancer is almost as brain-like as its appearance: albumen and fat are its main ingredients: the former in overwhelming proportion, the latter in varying quantity (sometimes very considerable) and in quality closely resembling the cerebral fats of the human subject.

The materials which during life run from the ulcerated surfaces of such a tumour are identical with those which *post-mortem* examination displays in its interior structure; and hence it is, that, in every instance of fungating sore, the microscope can inform us whether the discharge be the product of cancer, or of simple suppuration.

I have now described to you the ordinary characters of encephaloid cancer, sufficiently to furnish a text for such pathological remarks as I have to make on it; and sufficiently also to serve as a standard of comparison for the other two so-called species of cancer, *scirrhus* and *colloid.* I have sought to give chief prominence to the encephaloid form of the disease, because I believe it to be cancer κατ' ἐξοχην; because I believe it to be the highest and completest expression of that morbid tendency which constitutes the cancerous diathesis; because, in a word, I believe it to be of all cancers the most cancerous.

The distinctions of the other species are these: *Scirrhus* derives the sensible qualities which give it its name from its greater fibrousness of structure; there is spread through its substance a continuous uniform network of filamentous tissue, or a radiation of fibres from several separate dense centres, or a coursing of ligamentous bands, which branch and anastomose; and in the interstices of this rigid plexus, there lie microscopical elements, identical with those of encephaloid; identical (that is to say) with many of the cell-forms which I have enumerated, though not often presenting that excessive development which leads to endogenous cell-growth, or to the formation of large caudate cells; but showing, in preference, an abundance of those shapes which are transitional to filamentous tissue—spindle-shaped bodies, and nucleated fibres, in various stages of their growth. The scirrhous mass compounded of these elements is often very hard and tough, feeling like cartilage, and cutting like ligament; its

section shows a bluish-white colour, and seems glossy and semi-transparent where the mass is firmest; but, in points where softening is in progress, the surface appears more opaque and buff, presenting that yellow *reticulum*, or other yellow accumulation which I have already spoken of, as depending on an oily transformation of its material into the substance of compound granuliferous cells. I may add, that scirrhus is far less vascular than encephaloid cancer; that it grows less rapidly, and remains within much narrower limits of size; and that it is rarely the seat of interstitial hemorrhage.

Colloid deviates from the standard of encephaloid, usually, in a different direction to scirrhus. It is even less vascular than this disease; but, unlike it, it is often soft, gelatinous, or gummy: and yet this does not depend on the absence of fibrous tissue, for some forms of the disease have an exceedingly distinct filamentous framework: the softness of such specimens depending evidently on the peculiar nature and copiousness of that material which lies within their fibrous plexus, and which constitutes the bulk of the morbid mass. This characteristic material is a colourless, transparent jelly; in substance something like the crystalline lens; often as soft as the outer layers of that body, sometimes harder than its inmost layers: where scattered on membranes in the form of small rounded masses, it suggests to the mind the thought of a drop of quite colourless gum, fallen on the surface and dried there in its globular shape. A thin section of this extraordinary product shows in most instances that the gelatinous ingredient lies within very distinct loculi; often so distinct, that from this circumstance the disease has been named *alveolar cancer*. I should hesitate to say that, as a rule, the fibrous tissue is more developed in colloid than in encephaloid cancer; for, on the one hand, its greater perceptibility may be due, in a chief degree, to the extreme translucency of the intervening jelly, which sets these fibres off as though they were dried in Canada balsam; and, on the other hand, it is frequent to find specimens of colloid, in which (as in many of encephaloid) no fibrous network is perceptible, but in which the only trace or rudiment of matrix will consist in the faintest, almost imperceptible hyaline material, disposed reticularly, with some few elongated nuclei in the axis of its distribution. The intralocular material appears to me more peculiar in its physico-chemical qualities, than in respect of the organic shapes which occur in it. Sometimes a quantity of the jelly will seem amorphous under the microscope; sometimes ordinary round or oval uni-nucleated cancer cells, with fluid transparent contents, will be found; sometimes (though I doubt if this be not a partial admixture of alveolated encephaloid) a loculus will be full of simple cells, tending to become opaque with granular proteinous contents; sometimes a large granular mass, itself opaque, will lie amidst clear blastema, within a loculus, will be bounded by no distinct membrane, will not be resoluble into separate cells, but will contain a number of nuclei diffused in its substance; sometimes (though less often than is supposed) it will contain true mother-cells, having a smaller cell-brood within them; sometimes it will present chiefly naked nuclei

and nucleated fibres traversing its jelly at long intervals of distance, and associated probably with an abundance of oily globules; the latter elements may exist separately, or may be clustered in compound cells, or may be ranged in long branching lines which seem to follow the incipient fibrous organization of an interlocular matrix. All these ingredients are substantially the same as those of the other forms of cancer, differing only (so far as the eye can judge) as to the translucency and gelatinousness of the blastema in which they grow, and perhaps also as to the arrangement of their fibrous skeleton. With those other forms of cancer, moreover, colloid is ready to combine itself, and especially with encephaloid; which not only may unite with it in the construction of one tumour, but may arise as its secondary consequence, when colloid, as a primary disease, has contaminated the lymph or the blood.

With respect to the *habitat* of cancer (taking it again generically) the following, according to Rokitansky's large experience, is the order of choice in which the several organs of the body are primarily attacked by it—viz., most frequently the uterus, the female breast, the stomach, the rectum; next, the lymph-glands, the liver, the peritoneum, the bones; then, the skin, the brain, the globe of the eye, the testicle, the ovary, the kidney, the tongue, the œsophagus, the salivary glands. As regards the species—colloid prefers the stomach, the rectum, the peritoneum; scirrhus, eminently the female breast; next, the intestinal canal, and especially the stomach; encephaloid may occur in all organs, but there are some in which no other form of cancer ever exists—the liver, the kidney, the lung, the testicle, the globe of the eye, the lymph-glands; and it constitutes the only form in which a secondary development of the disease is known to occur.

Cancer may exist simultaneously in several organs of the body; but, where this is the case, we are generally able to distinguish, that in one organ its appearance has been *primary*, and that the other organs have suffered in *secondary* or *tertiary* succession. Its first outbreak is commonly in a single organ; and this first focus of the disease has a faculty, which in some respects is peculiar to cancer, of diffusing its contamination through other parts of the system. There are three methods in which this contamination may arise.

First, it seems probable that, even on simple continuous surfaces, the germs of cancer, if they alight and are retained, can fructify and lead to the development of a tumour; that is to say, that the disease can transfer itself by *immediate contact*. As regards serous membranes, you will find in Dr. Budd's work on Diseases of the Liver, some interesting cases cited, in which, as he thinks, a cancerous viscus in the abdomen has infected some opposite portion of peritoneum, or some portion beneath it in the abdominal cavity; occasional contact having caused the transference, or position having favoured the dropping of cancer-germs from one surface to another; and these, having been transplanted from one vascular surface to another, have become naturalized, and have grown in their new

relations. As regards mucous membranes, the same thing has appeared to occur on some occasions. Five or six years ago, I had under my care a patient, in whom, after death, I found reason to believe that the mucous membrane of the prostate gland had in this manner become infected by germs descending from an encephaloid kidney. Soon after the termination of this case, it happened that I received from the country for examination, a remarkably fine specimen of the same disease in the kidney; and, in laying open the ureters, I found along their mucous membrane some peculiar patches of excrescence, evidently of the same sort as the main disease. The mucous membrane was not destroyed; I could trace quite perfectly the continuity of its deeper layer; but superficially, and in separate pulpy patches, it presented this kind of cancerous efflorescence rising from its level. This was exactly what had struck me in the prostate of my previous case, where the substance of the gland was quite unaffected, and where the disease existed only as a growth of the mucous membrane. Some time afterwards, I mentioned the case at the Pathological Society, and Dr. Williams (its then President) informed me that, in cancer of the lung, he had occasionally seen similar vegetations arise from the mucous membrane in the bronchial tubes, traversed by the morbid expectoration; and very strikingly, he told me that, in cases where the progress of disease had forced the patient to lie constantly on one side of his body, he had noticed that these vegetations showed a preference for the depending side of the bronchial canal. On the whole, then, I think I may tell it you as highly probable, that, under favourable circumstances, cancer can propagate itself in the continuity of serous and mucous surface by the transplantation of germs.

Secondly, there is no point in pathology better established than that to which I adverted in a former lecture (the second), that cancer-germs, if by some lesion of the veins they are enabled to enter the circulation, will become centres of cancerous growth in the substance of whatsoever organ the blood may carry them to, and fix them in. This *intra-vascular development* of cancer is highly interesting, as the method by which the largest and most important secondary deposits are formed. And I may remind you of what I mentioned in my former lecture, that, so soon as the lungs or liver have become, by this first act of transference, the seat of a secondary deposit, they are very apt in their turn to furnish the nuclei for tertiary accumulations. You will readily understand how any germs that may have passed onward from the lung, and have reached the left side of the heart, having the aorta for their passage, and every branch of the arterial tree open for their distribution, will be able, with inconceivable rapidity, to affect simultaneously any number of organs in the body.

Thirdly comes that method of propagation which is effected by the lymphatic canals, and which consists essentially in transference by *continuity of blastema;* for, whatever may be the blastematous infiltration of any organ, the excesses of that fluid infiltration abound in its lymphatic vessels, and are liable, within them, or within the

adjoining lymph-glands, to undergo the same mis-development as would have befallen them in their original place of effusion. So far as one knows anything of the function of these organs, it may be said that their radicles are incapable of taking up anything that has shape; that they only fill themselves with fluid; and that they are so distributed in the body, as to saturate themselves at every moment with the interstitial fluids—that is to say, with the superfluous and unappropriated blastema of the parts in which they lie. Normally, this blastema is turned to account within the lymphatic system, by originating there the nuclei of the blood-cells. Now, lymphatics lie in cancerous organs as well as in healthy ones, and fill themselves with the blastema out of which *cancer* grows, just as they fill themselves with the blastema out of which brain or muscle grows; and it happens often that this cancerous blastema, in arriving at the next gland (where probably it is delayed) undergoes development there. I think this view more probable than the theory, that, with the lymphatics, as with the veins, the dissemination of cancer depends on the transference of germs; for the contamination of lymphatic glands occurs anteriorly to ulceration; and yet probably, without ulceration, the solid germs of the disease could not enter the imperforate tubules of the lymphatic system. I do not know that the distinction can be considered of much importance; but I think experience justifies it; for in encephaloid (where cells predominate) the veins are the chief means of systemic contamination; in scirrhus (where cell-growth is comparatively indolent), the lymphatics are more prone to suffer. And if it should be asked—How is it, on this theory, that the lymphatic glands ever escape? I think there are some very obvious answers. Some organs are very scantily supplied with absorbents, and in such, as, *e. g.*, in bone, the lymph-glands will rarely be contaminated; further, it may often happen that the lymphatic radicles are totally obstructed and spoiled for absorbent purposes in some early stage of the disease; and lastly, it must be remembered that the office of these organs is with *superfluities* of the nutritive exudation, and that, if the progress of cell-development in the cancer be one of great activity, there lies, in that very circumstance, a reason against the extension of the disease by means of a redundant blastema. The last point of this explanation is confirmed by what I have already stated, as to scirrhus preferring to transmit itself by the lymphatics, while encephaloid advances rather by the veins.

Whether any or all of these methods of propagation will enable cancer to be transplanted, like a parasitic growth, from the diseased organism to a healthy one—whether, in short, cancer is to be considered a communicable disease—seems hitherto not quite decided. Yet very nearly so; for physiological experiments have been performed again and again, and (with a single questionable exception) have uniformly failed to reproduce the cancer in a healthy organism, by those means of injection, inoculation, and the like, which, as I have explained to you, would inevitably have multiplied the disease in its original sufferer. The amount of our certain knowledge on

the subject, accordingly stands thus: within the organism of a person suffering from that cachexia which establishes a cancerous tumour, any transference of cancer-germs from one vascular surface to another, or any transferable excess of shapeless blastema in the seat of the primary disease, may lead to the formation of new centres of cancerous growth in certain definable localities; but there is no evidence, and little probability, that the same transferability of the disease relates to any other organism not under the influence of the specific cachexia.

Thus far, gentlemen, I have spoken to you of the shapes and sizes, the colours, the degrees of consistence, and the molecular construction of tumors. Tegumentary, vascular, fatty, fibrous, cartilaginous, bony, cystic, cancerous: these are the several adjectives which I have found it convenient to take as heads, for describing to you the purely anatomical characters of certain morbid enlargements. But your patient consults you, gentlemen, not with a view of making preparations of himself—not for abstract information whether a particular lump on his body be made of fat, or of bloodvessels, or of growing cells—not to know how it looks under the microscope; but in order that you may inform him, or at least that you may yourselves be informed, what it is in relation to his health and life—what it is in relation to your power of curing it. And now, in pursuance of my plan, I purpose reviewing with you such pathological considerations as determine an answer to these questions. I purpose analyzing the subject in that more practical and more rational manner, which consists in contemplating and classifying tumours according to the morbid actions which they render evident in the living body.

First of all (for I take the easiest first), you will have no difficulty in dealing with tumours dependent on distension of natural cavities or ducts. In speaking of cysts, I explained to you how the so-called encysted tumours of the scalp arise in this manner: how the orifice of a follicle gets plugged; how, then, the secretions in the body of the follicle go on; how the follicle becomes a little sac; how that little sac grows bigger and bigger, getting strengthened by growth in proportion to its stretching; and how the largest wens we meet with—wens almost as large as the heads they grow on—can commonly be proved to have had this microscopical commencement. In a case of this kind, pathology and practical experience would concur in pronouncing the tumour to be one of purely local causation, to be one indicating no impairment of general health, nor (while in the state of tumour) capable of producing any such impairment. Its evils would be purely local.

There are many other tumours of similar origin; not, indeed, owing to the morbid closure of any excretory channel, but to an increase of the normal secretion within a cavity which is naturally closed—*e. g.*, within the tunica vaginalis, forming hydrocele; or within the bursa patellæ, forming housemaid's knee; or within the Graafian vesicles, forming simple ovarian cysts; or within the shut sacs of the thyroid gland, forming bronchocele.

In these instances, as with the follicle first spoken of, the tumour consists in the distension (sometimes an enormous distension) of a secretory cavity by its own excessive product.

Let this, then, be your first class—*tumours by accumulated secretion;* and remember that they may arise, either in vesicular structures, by a redundant and hypertrophic activity of the secreting function, or in follicular structures, by a mechanical retention of the secreted material.

Then, in marked contrast to these tumours, which are all partially and some entirely of mechanical origin, come others which are eminently the result of a vital process—enlargements, not by passive distension, but by active growth. And in my last lecture, as I enumerated many instances of such growth (although I then carefully avoided anything like a general statement on the subject), it no doubt struck you that, among these instances, there were several which partook intimately of the nature of hypertrophy.

Let us look at this in detail. In *tegumentary tumours*, we found a projection and prolongation of the skin, or mucous membrane; sometimes with a narrow peduncle; sometimes broadly attached; sometimes with disproportionately large development of subcutaneous fat; sometimes with no such development; but always, as the essential thing, *skin in excess.* In *vascular tumours* we found a plexus of bloodvessels preternaturally grown; sometimes nearer to the arterial inlet of the part, and consequently presenting pulsation, with some other similitude to aneurism; sometimes nearer to the venous outlet of the part, and, accordingly, possessed rather of the characteristics of varix; but, whether one or the other—whether arterial and pulsating, or venous and stagnating—in either case we found these erectile or vascular tumours consisting essentially of *vessels in excess.* In *fatty tumours* we found an accumulation (sometimes to an immense extent) of adipose tissue; of tissue quite undistinguishable, in all anatomical and chemical characters, from the elements of normal fat structure amid which it rises; we found that these tumours never grew in situations, naturally destitute of adipose tissue—that, accordingly, where they rise, we may identify them as *adipose tissue in excess.*

So, speaking of this group of tumours (the fatty, the vascular, and the tegumentary) we may generalize their more important common characteristic as *partial hypertrophy;* there is over-development of a particular solid structure of the body; but that act of over-development does not spread itself coextensively with the structure; it limits itself, usually, to some single patch or segment of the structure it invades, and there exhausts itself.

We cannot always trace the local momentum, in which these acts of partial hypertrophy arise; but that the momentum is a local one seems obvious; first, from the *singleness of site* usually chosen, and *singleness of tissue* universally chosen, by the disease for its manifestation; secondly, from our empirical knowledge that the removal of such tumours constitutes their cure. The patient with fatty tumour is by no means necessarily obese—the patient with nævus has no

general erectility: the disease does not seem, like carbuncle, or gout, the concentration of a constitutional humour in a particular part, but (as I said before) purely the act of the part itself.

Sometimes, it is true, there exists a disposition to plurality of these tumours: you see several nævi, or several lumps of fat, or several flaps of pendulous skin, developed on the same person; and in such cases (which, however, are by no means common) you might be disposed at first to impute a humoral origin to the disease—to think that some idiosyncrasy existed in the person's blood; that, to account for this excessive evolution of fat vessels, or skin, there must prevail some excess of the materials out of which Nature elaborates these textures. But I would rather believe that in such cases the obscure cause of the multiple hypertrophies resides in the tissue itself, not in the blood; that the nature of the momentum tending to overgrowth is the same in these several centres of its action, as when the product is single; that the difference is but one of number; that the essential thing is a peculiarity in the mode of growth—a developmental peculiarity, in one tissue of the body, which may have a single centre of manifestation, or several centres.

In the fœtus—where no humoral disease can exist otherwise than through the mother, and in cases where no such maternal blood-disease had existed—the integument of the body has often undergone faulty development; being either redundant, so as to form pendulous flaps, or tight and scanty, so as to make constrictions; and since it is obvious, or at least highly probable, that in these instances the peculiarity of growth must be inherent in the tissue itself, they will serve for some illustration and evidence of the view I have just taken of uni-textural hypertrophies in the adult.

I may add, too, in respect of the growths under our consideration, that, whether they be single or several, their surgical removal is curative; they do not reappear in other parts of the body.

Some of the instances which I have already mentioned, but still more some which we have now to consider, will excite your attention to the necessity of establishing a third pathological group. It is particularly in respect of the hard tissues—the fibrous, the cartilaginous, and the bony—that we have occasion to notice tumours which are *hypertrophic*, it is true, but hypertrophic in a particular sense. You find, for instance, a bony tumour developed in connection with the inner condyle of the femur: if the material of that bony tumour were diffused equally throughout the whole bone, you would have a case of general hypertrophy of the femur: if it were concentrated in the inner condyle, rendering that portion much larger than it should be, you would have a case of partial hypertrophy of the femur; but, in the case supposed, the superfluous material forms an exostosis or osteophyte; it is not deposited interstitially, so as to enlarge the condyle in its original type of construction, but is added to it by simple interior propinquity; and thus you get a case of what I may call *adjunctive hypertrophy*, or *hypertrophy by apposition*.

Under this category you would range not only most cases of bony tumour, but, quite as remarkably, the fibrous tumours; and, on the

principle of *hypertrophy by apposition*, you will have no difficulty in understanding why these tumours should particularly affect the uterus, the dura mater, and the mammæ; organs which, being themselves eminently fibrous, become natural centres and foci of fibrous hypertrophy. And further, gentlemen, with reference to these modifications of nutrition in the more solid parts of the body—in the organs of support, I may remind you that fibrous tissue, cartilage, and bone, stand in a peculiar relation to each other. They have reciprocal affinities of a very marked kind: in the successive improvements of organization, as you ascend the animal series—in the successive steps of progress that constitute the development of the embryo—you see one of these tissues holding the place and fulfilling the functions of another, or actually undergoing transformation into it. They are susceptible of conversion into each other; they are, so to speak, anatomical equivalents each of the other.

See, for instance, cartilage acting as bone in the skeleton of the lower fishes; even inclosing their nervous centres, and fulfilling all purposes of our stronger skeleton. See how it does the same thing in the embryo and young animal of the highest class, and how gradually, even in the human subject, it yields to ossification. See, again, how easily slight errors of nutrition convert into bone cartilages meant to be permanent, such as those of the larynx and ribs: see fibrous membrane, equally with cartilage, constituting a natural matrix for the development of bone, as in the cranium of the fœtus, and observe how easily the same tissue undergoes abnormal ossification, as in the tendons of birds, or in the dura mater of the human subject. It accordingly appears to me that, without any straining of analogy, a cartilaginous tumour may be spoken of as a hypertrophy of the bone, or of the fibrous tissue with which it is connected; or a fibrous tumour connected with cartilage or with bone may be spoken of as its hypertrophy; or a bony tumour, evolved in connection with cartilage or fibrous tissue, may similarly be spoken of as its hypertrophy. Within certain limits, then, it would appear that partial hypertrophy, whether interstitial or adjunctive, is compatible with the production of a material, not indeed absolutely identical with the parent texture, but closely akin to it in use, and commutable with it in development.*

With respect to the primary origin of those various tumours which arise in a process of hypertrophy by apposition, with or without conversion of tissue, just as with respect to the simpler cases of partial hypertrophy, I see no reason, either in pathology or in practice, for admitting the necessity of any constitutional taint, as a pre-condition of their growth. On the contrary, while analogy would lead me to believe that cartilaginous, bony, and fibrous tumours (being essentially hypertrophies) must have their origin in local conditions, I find this view additionally confirmed by the practical fact, that, when such tumours are surgically removed, or still more

* In the general hypertrophy of synovial membrane, I have repeatedly had occasion to notice, microscopically, the abundant development of the elements of cartilage, and also to obtain chemical proof of their presence.

certainly, when that part of the body from which they grow is removed, we are able confidently to predict against any reappearance of the disease.

Finally, gentlemen, the difficult task remains to me of setting before you the pathological affinities and contrasts of *Cancer*. Let me remind you that I use the word generically; including under it the three species of which I have spoken, and taking the encephaloid form as its most perfect and characteristic illustration.

Fix your attention, first of all, on the total unlikeness of cancer to any kind of tumour we have hitherto considered: observe how impossible it is to regard cancerous growths as accumulated secretion of any organ in which they arise, or as the results of its hypertrophy either interstitial or adjunctive. They are distinctly new products —new developments of the organism; and they correspond to some new purpose. The evolution of a cancerous tumour in the body marks, I apprehend, a new state of things in respect of the patient's total organization and vitality; just as much as the first acting of the kidneys in the embryo, and of the lungs in the infant, respectively mark new eras in the animal's progressive development.

Thrust aside all the accidents and trivialities of the subject; strip the question naked; and what does a cancer mean? Substantially it is a new excretory organ. Under the pressure of some mysterious constitutional necessity, a growth arises which (in its typical form) tends essentially to acts of eliminative secretion; just as distinctly as the healthy liver or the healthy kidney. You must not stop short at the *tumour:* you must scan the whole drama of the disease in which the tumour forms but a prooemium. Look again at such a case as I gave you for illustration—a case of encephaloid manifested in the globe of the eye: that vast fungating ulcer which ensues on the protrusion of the tumour, and which continues hourly to purge forth its profuse discharge—that is the real intention and purpose of the tumour, as palpably as urine expresses the intention of the kidney, or bile the intention of the liver. The cells of the tumour have grown like healthy gland-cells—like the nucleated cells of a mucous membrane, only to discharge themselves with their contents. There is nothing, I repeat, like hypertrophy in the disease: it consists essentially in the establishment of a new vent—a new organ of elimination; and that organ develops itself according to the type of other secreting organs; it develops itself as an apparatus for the formation of deciduous cells.

How constitutional—how intensely constitutional—is this eliminative action, can hardly be misunderstood. The mere fact that Nature thus (if I may say so) deliberately, and without any exterior provocation, organizes in one spot of the body a drain which becomes so ample as to starve the remainder; the circumstance that this flux is not a single emptying out of some previous local accumulation (such as one sees in the pointing and discharge of an abscess), but is a persistent process, depending day by day on new acts of growth; the observation that the tendency to the disease is in many instances hereditary; the existence of a marked cachectical state which pre-

cedes, as well as accompanies, the evolution of the tumour; and, most of all, that flagrant evidence of metastasis* which daily renews itself for our instruction, consisting in the failure of surgical operations, by reason of the obstinate emergence of the disease, even again and again, in parts previously uncontaminated by its presence;—these arguments are to my mind as conclusive for the constitutional and purely constitutional origin of cancer, as any which I could adduce to show you the constitutionality of smallpox or gout.

Thus much is beyond question. And, while I tell you that a cancerous tumour is an organization for excretory purposes, I wish I could go further, and could explain to you what is that mysterious condition of system in which this eliminative effort has its root; what it is that enables and induces the blood thus to starve those various organs which are the natural claimants of its substance, and thus to waste itself in works of supererogation. We have seen parasites acting thus by the body ; we have seen the blood involuntarily yielding up its richness to their extraneous suction. But here the case is quite different; the blood seems (if I may use the phrase) spontaneously and voluntarily, and under no pressure of local circumstances, to set about constructing an organ for the appropriation and discharge of its own blastema. It is from sedulous chemical investigations alone, that we can hope for light on this most difficult subject; from such investigations, I mean, as will compare the total chemistry of the cancerous body—blood, tumour, excretions—with the total chemistry of the healthy body; and especially will found themselves on an exact and comprehensive knowledge of those natural changes which occur in the progressive and regressive metamorphoses of the blastema of the blood. Hitherto, the chemists have done nothing for us in respect of this disease; and till they have furnished us with the formation just indicated, our hopes of cure must necessarily remain dormant, or must content themselves with speculative and empirical endeavours. For pathology distinctly traces a chemical function in the disease, and shows that it is from the basis of chemistry alone that any rational cure of the disease may possibly be argued out.

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* I am content to rest my justification of the word "metastasis," on the habitual return of the disease after operations, even when they have been performed with the best apparent prospect of success. But a case is quoted, on the authority of Parent-Duchatelet, which looks more like what is commonly recognized as *metastasis*—namely, that the disease spontaneously deserts one site and simultaneously addicts itself to another. As a solitary instance, it adds little or nothing to the evidence of surgical practice; but I transcribe the case for its curiosity: "A woman—after having for a length of time suffered from tumour in the breast, which possessed all the characters of non-ulcerated scirrhus, and after having presented the symptoms of cancerous cachexia in so marked a manner, that Dupuytren not only refused to remove the diseased organ, but dissuaded Parent-Duchatelet from the use of leeches—was seized with remittent cephalalgia of intolerable violence; at the same time the mammary growth ceased to be painful, and eventually disappeared almost completely. Apoplectic symptoms with hemiplegia supervened, were combated with the ordinary means, and recurred twice before the patient's death, which took place ten weeks after the first apoplectic seizure, and two years after the supervention of the symptoms in the breast. On *post-mortem* examination, a tumour of the size of a nut, and possessing (according to Cruveilhier) the characters of carcinoma, was discovered floating, as it were, in a quantity of diffluent brain."

In the ground we have gone over, you will have seen what it is which constitutes the so-called *malignity* of cancer, and which assigns it a separate place and higher importance in the list of morbid growths; this, namely—that the cancerous tumour is a mere symptom of constitutional disease, a mere phenomenon, locally arising in a concentrated act of the entire system, as demonstrably and as simply as a paroxysm of gout is the local product and local evidence of a general disorder.

You will, perhaps, think these expressions strong; and you may be inclined to ask—when an encephaloid eye, or testicle, is removed, is it as though one should amputate a gouty toe during its paroxysm of specific inflammation? Making allowance for the difference between *acute* and *chronic* manifestations of a general disease (for this allowance is of course necessary in drawing a comparison of gout and cancer) I fear the two cases are much more alike than is generally believed. There is one substantial difference, throwing a little advantage on the side of the cancer-operation, and I will tell you directly what that difference is; but first let me point out to you a fallacy which sometimes may affect very sensibly your estimate of the success of such operations.

With regard to a gouty toe it might happen (surely rather by chance than skill) that the adventurous operator should step in at a moment when the disease had exhausted itself; when Nature had done with the toe all that she meant to do with it; when the period of quietude and convalescence had arrived. The lucky amputator would gain the credit of this coincidence; but how rarely would such a chance occur! how much more frequently would the patient undergo additional suffering in consequence of that rash mutilation! So with cancer: Surgery, perhaps, at times, gets the credit of cures which Nature had already achieved; and sometimes, perhaps, owing to blunders and uncertainties of diagnosis, the non-return of cancer after operation has depended on its non-existence before the operation—on the supposed cancer having been a fibrous or sero-cystic tumour, or some mere inflammatory swelling.

But I have said that there is a real difference between the cases: I will now explain it, for in some respects it is important. Gout reappears with extreme facility, because it can develop its chemical product in almost any tissue of the body, and does not require that any special organization should exist, in order to the local fixation and discharge of lithic acid. The unknown albuminiform material of cancer, on the contrary, does require such an organization for its discharge; it requires a cell-growth for its purpose, and it is at the least doubtful whether it can avail itself of any normal cell-growth in the body; whether it can *cancerize* any existing cells; or whether it must not start *de novo*, and begin by organizing a set of cells for itself. Whichever of these two possibilities may be the case, I can at least tell you this: if you remove a cancer, say of the lip (under circumstances not of extreme malignity) and if no traces of cancer structure are left behind, either in the wound or in the lymphatic glands, you oppose a real check to the disease; it may not be more than this, but

this much it certainly is—a check; but if any trace of cancer-structure be left—say in a sub-maxillary lymph-gland, the morbid action transfers itself there as easily as the function of one kidney would repeat itself in the other, and the disease is quite unaffected in its progress. And the history of secondary cancer altogether illustrates the same point: a few grains of cancer-tissue passing into the circulation, and becoming fixed in the liver or the lung, will rapidly determine there the evolution of encephaloid masses; although, on the one hand, those masses would not have grown there without the adventitious aid of transplanted germs; nor, on the other hand, would those germs have produced the same phenomena of growth, except in some subject of the cancerous cachexia. I infer from these premises, that the formation of a cancer in the body is not so easy and off-hand a process as the local determination of gout or rheumatism; I infer, either that a special cell-growth is necessary, which it takes time, with some intensity of cachexia, to construct; or at least that the existence of such a cell-growth promotes, in a remarkable degree, the ulterior development of cancerous phenomena; and, in either case, that the system will tolerate a not inconsiderable degree of whatsoever conditions form the cancerous diathesis, without proceeding to construct a cancerous tumour *de novo*, when every atom of its primary structural manifestation has been thoroughly removed from the system. Even in gout, where the facility of localization is comparatively great, we know how long a time may elapse, and how much general illness may arise from gouty blood, before the disease first succeeds in centralizing its products at the toe, or elsewhere; and if that toe were removed, there would probably be another lengthened period of latency, before a new focus of gouty inflammation could be established. And this difficulty exists, as I have said, to a much greater degree in regard of cancer, owing to its requirement of a special structure for its eliminative acts; whence we may confidently argue, that cancerous diseases have a chronic period of latency, during which their cachexia acquires intensity from accumulation, till at length it suffices to establish the local vent; and we may argue further, that the disease can be again reduced to this state of latency and to the accompanying difficulties of evolution, if all such local conditions be removed as favoured the first localization of its products. And here lies the practical importance of these considerations; for it is exactly in that chronicity which we have traced in the constitutional disease, and in the reluctance with which Nature proceeds to a total reconstruction of the cancer-growth, that the chance (such as it is) of doing good by surgical operation, singly and entirely consists. And the whole tact and discrimination of the surgeon, in deciding whether an operation may probably lead to the patient's relief, have to be brought to bear—first, on determining the total absence of any secondary deposits, or any irremovable extension of the growth, which might serve as a centre of new development; and secondly, on measuring the intensity of the constitutional cachexia.

In respect of the latter point, there are many obvious considera-

tions, as to the rapidity with which the tumour has been evolved, as to the state of activity in which it actually is, as to the patient's apparent general health, and the like. But I pass over these topies (as better adapted for clinical illustrations) in order to suggest to you the sort of guidance which you may derive from the site of the disease, from its speeies, and from the amount of local influences apparently concerned in its production.

As respects the pathological relations of the forms or species of cancer, each to the other, it seems to me that the cancer is a perfect expression of the cachexia in which it arises, in proportion as it contains the means of fulfilling its eliminative destiny. Encephaloid consisting entirely of cell-growth, and hastening to discharge itself, seems the most characteristic representative of what is fatal in cancer—a view additionally confirmed by its rapidity of evolution, and by the empirical evidence of its habitual return after operation. Of colloid, I can scarcely offer an opinion; it is too rare, especially in surgical practice. Scirrhus I apprehend to be the lower manifestation of the disease; and in proportion as the scirrhous character predominates in a tumour—in proportion as the blastema has suffered itself to undergo a fibrous transformation—in such measure I cease to recognize that which is distinctively cancerous and malignant. In this respect, I would compare encephaloid and scirrhus, in their mutual relations, to the fibre-forming and cell-forming sequels of inflammation; the intenser inflammatory acts running into the pure cell-forming process of suppuration; while the less intense inflammatory acts deviate into the slower construction of fibre.

I will not venture to deny that local conditions may check the development of cells, and may thus interfere with that free eliminative process, by which the cancerous cachexia seeks to relieve itself; and the disproportionate excess of nucleated fibrous material may sometimes possibly indicate some such local influence, thwarting the general tendency of the disease, and preventing the local structure from being an adequate expression of the constitutional fault. But —were it not for this possibility, I would venture to say universally (and even with this qualification, I would say generally) that the nucleated fibrous material will be abundant in proportion as the malignant cachexia has exhausted itself; that fibrous transformation so far as it extends, illustrates the operation of common, not of specific, developmental influences in the part. So with regard to those compound granular corpuscles, constituting the yellow softening material in cancerous growth, there seems no difficulty in adopting the view (lately urged by Virchow) that these bodies represent the degeneration of cells, and consequently, *cæteris paribus*, evince a retrogressive tendency in the effusion where they occur. If we may consider these two points established—that fibre, *quoad* its existence and quantity, illustrates an abortion of the cancer-growth—that compound granular cells, *quoad* their existence and quantity, illustrate an exhaustion and retrogression of the morbid influence, we possess some material in pathology (though not always applicable in practice) for guiding our prognosis as to the probable

recurrence of the disease. The lesser malignity of scirrhus, however, loses much of its relative advantages in fact, from the circumstance of its ready diffusion, by continuity of blastema, to the adjoining lymph-glands; and as I have already told you, the presence of a single batch of cancer-cells in a lymphatic gland is quite sufficient to insure for the cachexia every needful opportunity of development —quite sufficient to forbid the hope of any prolonged period of latency.

Next, as regards the inferences which may be drawn from the evidence of local causation in the origin of cancer—there is a belief that blows often cause it, that it follows inflammation or functional excitement, that it invades erectile tumours, and the like. In regard of this belief it appears to me that its preference for particular organs, or for organs in a particular state of action, admits in some respects of being generalized in a ready explanation. The part most readily selected for the invasion of cancer, the *pars minoris resistentiæ*, will probably, in many instances, be one previously the seat of hyperæmia. The uterus and the breast, with their frequent fluctuations of nourishment; the lip, or the tongue, or the stomach, which for years has been kept in a state of irritation and over-vascularity by local circumstances; the part which has suffered effusion from a blow; the vascular tumour, with its superfluous blood;—such are the organs in which cancer most readily makes its first appearance. And for this obvious reason: the disease has to develop itself out of blastema, furnished by the blood for the materials of its nourishment; it has to compete with the assimilative acts of the several healthy organs of the body; and it chooses, in preference, any structure where, by previous contingencies, the necessary materials for its growth may accidentally be present in excess.

As respects local influence, we may perhaps be justified in stating thus much: that circumstances of topical irritation and hyperæmia will enable cancer to localize itself under a less intensity of cancerous cachexia than would else be necessary for the origination of the process; that, except for such local facility being afforded to it, the cachexia might have remained latent, or at least might never have realized its critical and evacuative tendency; that, for instance, a chimney-sweep, except for the local irritation of soot, would not have had cancer developed in its scrotum, and might not have had it developed at all. And in these cases, where we can distinctly recognize the influence of exterior irritation in promoting the evolution of the disease, and where (as occasionally happens) we can believe that the cachexia would have been insufficient for that effect, except for the adventitious aid thus given to its feebler intensity; in these cases and on these principles it is, that surgical interference is often eminently useful, by depriving the cachexia of the local advantage it had gained. It is peculiarly in respect of cutaneous cancer, and cancer of the tongue, that this line of argument applies; and I may mention to you, that, in these instances of the disease, there is a still further illustration of the low intensity of the cachexia, seeing that the formation of new structure is always here at its

minimum; that the development of true cancer-growth is always peculiarly slight; and that here (if anywhere) it is, that the previously existing elements of the tegumentary surface are used for the eliminative action of the disease. For what is called epithelial cancer is, in regard of its function, as true a cancer as any; cancer of the lip or of the tongue is as unquestionably an evidence of the cachexia, though not in so high a degree as fungoid testicle would be; and yet, in its examination, we often are unable to discover any elements but such as we might ascribe to epithelial hypertrophy.

It cannot but be obvious to you, that to speak of *curing* cancer by operation is an absurdity; and if you reflect pathologically on those cases in which the excision of a cancerous tumour (for instance, from the female breast) is declared to be admissible, you will find that, in the majority of them, the permission to operate implies also that there is not much to cure. For you would endeavour by operation to reduce the disease to a state of latency, only when the slowness of its progress, its tendency to fibrous transformation, the influence of local causes in its production, and the absence of marked ill-health in your patient, had concurred to give you an assurance that the cachexia existed in its weakest form, and with the merest sufficiency of power to maintain the indolent local disease. Now, in such a case as this very little is gained by an operation, unless the tumour be on the point of ulcerating; hardly enough to compensate the patient for the pain, much less for the risk of a capital operation. Under such circumstances as I have alluded to, scirrhous masses remain indolent for years, sometimes for the whole remaining lifetime of the patient; and the survival of persons from whom such tumours are removed would have been equally prolonged without the interference of the surgeon. I make exception of cases, however chronic they may have been, where the tumour is on the point of ulcerating; because here (provided other circumstances render the operation admissible) the further quiescence of the disease is rendered probable by removal of its local manifestation, and the patient is saved that excessive increase of suffering, and that greater imminence of danger, which belong to the ulcerated condition.

To undertake a capital operation under opposite circumstances—with a tumour markedly encephaloid, evolving itself rapidly, without local causation, and with evident impairment of health, is a proceeding which cannot be justified therapeutically. A patient's importunity, sometimes perhaps aided by his surgeon's partiality for operations, will often introduce into consultations on these subjects the phrase of "giving him a chance," as if there were anything like *chance* in the matter—anything but the gloomiest of all possible *certainties*. The supposed gain in such cases is that of prolonging life a few months—for I believe no competent authority will venture to promise more; and this advantage is materially counterbalanced, if not neutralized, by the risk inseparable from the larger operations of surgery, and by the possibility that chloroform, hemorrhage, erysipelas, purulent infection, or some other mischance, may suddenly deduct from the patient's life at least as many months as one

hoped to add to it. Circumstances occasionally arise, which make the endeavour for a few months more life a consideration of supreme importance, and morally warrant the operation; but you should never lose from your sight the danger of an immediately unfavourable event to this endeavour; nor should you ever refrain from explaining that danger clearly, and precisely, and considerately, to your patient.

To remove a cancerous tumour partially, or to leave some secondary formation in the lymph-glands, or elsewhere—is, as I have explained to you, simply to transfer the manifestation of the cachexia from one spot to another. It will advance at the new spot with neither more rapidity nor less rapidity than in the morbid mass which has been removed.

The removal of such smaller cancerous growths as do not fall within the category of capital operations, is governed of course by the same pathological principles; with exception, however, that what the French call *operations de complaisance* may often be undertaken with propriety; and it would under most circumstances be allowable to remove any small cancer of the tongue, lip, scrotum, or penis, even when the adjoining lymph-glands are contaminated, because the transference of the disease would be an advantage to the patient, who would suffer less inconvenience from the secondary growths than from the further extension of the original ulcer.

There used to prevail an opinion, that operations for cancer were successful in proportion to the earliness at which they were undertaken. This is true in respect of such cancers (especially epithelial cancers) as have had their growth obviously favoured by circumstances of local irritation; but as regards cancer generically, both pathology and surgical statistics assure us, that such an opinion must not be admitted without very considerable qualification by other circumstances, to which I have adverted.

LECTURE IX.

Scrofula: tubercle its essential and diagnostic product; distinction of scrofula from sub-inflammatory and atrophic processes occasioned by mere debility; experiments on the artificial producibility of tubercle. Hereditary transmission of scrofulous diathesis, as a developmental peculiarity; material of tubercular deposits; its microscopical characters; is it an inflammatory product? Organs preferentially invaded by tubercle; its anatomical relations to the natural structures; diseases with which tubercular deposition is incompatible; diseases with which it has affinity: fatty degenerations; pathological generalizations as to tubercle and the tubercular diathesis; contrast with cancer; therapeutical influences against tubercle.

Gentlemen: For the subject of to-day's lecture I propose to consider *Tubercle;*—meaning by the term that unorganizable deposit which occurs in various organs of the body under the influence of a peculiar constitutional state—marking such a state, and rendering it specific, by the name of the *Scrofulous diathesis.*

In this country, at least, you can have no more interesting object of study. The frequency and the fatality of the disease constitute its importance. If you look at the Registrar-General's statistics of mortality in the metropolis, you will see that among the specified causes of death "tubercular diseases" hold the chief place. He assigns to them about a fifth of the total mortality; and when you consider how very many instances there must be of disease in internal organs due to tubercular deposit, where the nature of the morbid process is unrecognized, and where consequently the cause of death is recorded by the mere mention of its site—as "disease of the brain," "disease of the kidney," "disease of the lung"—when you consider, besides, how many other fatal diseases may be derived, indirectly, from the same deposit, or the same diathesis—you will be able to measure for yourselves the vast importance of acquiring an accurate knowledge of influences so hostile to life.

Already, in the first words of this lecture, I have spoken of tubercle as the specific product of a peculiar constitutional act; and in order to insure accuracy of phrase, no less than for the sake of pathological exactness, I would recommend you to employ the adjective "scrofulous" only when you mean "essentially associated with tubercular deposit."

It may hereafter appear—at least I will not venture to assert the contrary—that other manifestations of disease may admit of being classed in an equally close relation of dependence on the same constitutional state; but at present there is no evidence to justify us in extending to other diseases the particular formula which includes the pathology of tubercle;—this, namely; that under the influence of a constitutional bias, which is peculiarly susceptible of hereditary transmission, and peculiarly difficult of artificial genera-

tion, there occur local deposits of an organic material, which is insusceptible of ulterior development.

In order to clear the ground, I shall begin by speaking of some of those conditions to which the name has been—I will not say wrongly, but incautiously and vaguely applied.

Manifestations of the scrofulous diathesis very frequently occur in connection with a state of general debility—with such a state, I mean, as consists, not in evident failure of muscular strength, but in depression of the vital power, in imperfection of the nutritive processes, in defective resistance to injury and to disease; and, *in respect of these conditions*, we constantly see tubercle associated with other phenomena, which belong to it merely by reason of that accompanying weakness—belong to it accidentally, not essentially. These phenomena—the accidental associations of scrofula—admit of ready reproduction and imitation, by experiments which are merely debilitating. They are essentially temporary, or rather are essentially coextensive in duration with whatever debilitating causes may have produced them; and (so far as I know) they do not evince the slightest tendency to hereditary transmission.

Look, for instance, at Majendie's well-known experiments, as to the influence of non-nitrogenized diet, and other insufficiencies of nutriment. Ulcers of the cornea, leading to destruction of the globe of the eye, were observed by him to arise uniformly in connection with the emaciation and the impoverishment of blood produced under these circumstances.

From my own observations I can confirm the accuracy of these statements. In animals exposed experimentally to such causes of disease, I have again and again seen various ulcerations arise in the cornea, the stomach, the intestines, &c.; and the dietetic causes have seemed capable of acting with increased effect, when their debilitating influence has been assisted by confinement in damp, dark, and ill-ventilated places.

Now, in the practice of medicine and surgery, these disorders of defective nutrition play a very important part. The various slighter forms of chronic inflammation with which we are familiar—the sore eyes, the sore ears, the sore noses, the sore legs, the whitlows, the congested and catarrhal mucous membranes, which are so frequent among our hospital patients; all these, I repeat, may be readily produced under the artificial influence of defective nourishment. True—that they *may* occur in connection with tubercular disease; the subjects of tubercular disease are, in fact, from the reasons I have mentioned, very liable to them; but, on the other hand, any amount of tubercle may exist without these accompaniments; or they may exist to an unlimited extent without the slightest trace of tubercular deposit in any part of the body; and experiment on the lower animals, which so easily produces the one class of derangements, can hardly be made to produce the other. As it requires the passage of, at least, some generations to form a variety of the human race, and to fix and render hereditary the conformation of a Caucasian, or a Carib, or a Bushman; so it takes time to establish

and render permanent the scrofulous or tubercle-forming diathesis. While I entertain no doubt that it is artificially producible, yet I am persuaded that its producibility by experiment has been immensely overrated. The difficulty of producing it in any one generation, free from the taint, amounts almost to impossibility; unless change of climate be added to the other conditions of the experiment. The influences by which scrofula has become a permanent element in human society, have probably affected several generations in succession; and are in their nature such as, if concentrated on one generation, would not produce tubercular deposits, but would rather destroy life by the local inflammations above mentioned, or by certain other deposits or degenerations, which I shall presently mention as standing in very close affinity to the tubercula.

I do not hesitate to confess that knowledge on these subjects is far from perfect, and you will understand that future observation may correct what I have stated, and may give certainty where hitherto we have but doubt; establishing, perhaps, a nearer connection than is yet seen, between tubercle and the transitory effects of defective nutrition. I would, however, strongly recommend you, in the present state of our information, to confine your use of the word "scrofulous" to such diseases only as are attended with those deposits most characteristic of the diathesis.

Having spoken of experiments performed on the lower animals, I feel bound to caution you against a too implicit belief of all you may read in books as to the experimental production of tubercle. Statements on this subject have been made and disseminated too hastily. For instance, rabbits are cited by authors, as peculiarly prone to become subjects of the disease. "A rabbit, fed in a damp, dark cellar, on watery vegetable food, (says Mr. Phillips,) soon becomes the victim of tubercular deposits." "There are certain influences (says Dr. Walshe) "which experience has proved to lead unfailingly to the development of tubercle in the liver of rabbits." Four or five years ago, when I was busy with experiments on this subject, I received from a friend the so-called tubercular liver of a rabbit; the deposit was white, not very firm in any part, and in some spots diffluent; it extended in several directions throughout the thickness of the organ, reaching its surface, and bulging it at various points; but there was something in its appearance which struck me at first sight as unlike tubercular deposit; it appeared continuous in lines, rather than in masses; it seemed to branch, too, in the direction of the ducts, as though it were dependent on their anatomical arrangement. I proceeded to examine it with a high power of the microscope, and found, to my astonishment, that the whole mass consisted of the minute oblong eggs of some entozoon. The fact seemed likely to be of importance, and consequently I followed up the observation by others. On inquiry of a *candid* poulterer (for the sellers of eatable stock are naturally reluctant to admit the possibility of disease in their animals) I found that these "tubercular" livers are common—very common; that they will be found often in almost every tame rabbit cut open, and in litter after litter; and, strangely

enough, that they do not appear incompatible with good health, or at least with health sufficiently good for market purposes. Now, I examined dozens of these livers, always with the same result; and I may mention to you, as of some interest in relation to the habits of the entozoon, that while engaged in these examinations, I found the same ova in the gall-bladder and in the whole length of the intestinal canal; in several parts of the latter (as *e. g.* in the cæcum) I observed them actually following the inflections of the mucous membrane, and lining its follicles almost like an epithelium.

In continuation, I made various experiments, to see if I could produce tubercle artificially, and various other examinations to see if I could find it in rabbits dying under other circumstances. The result may be told in a word: I have never seen tubercle in a rabbit. I do not wish you to infer from this, that rabbits are insusceptible of the disease; my knowledge by no means extends to this; there may have been some share of accident in my non-observation of tubercle among so many specimens; and other more fortunate observers may have witnessed the disease, perhaps frequently. But what I would insist on is, that the artificial producibility of tubercular deposit is by no means the simple and straightforward process it is supposed to be. So far as the belief in it depends on such statements as I have cited to you, I feel bound to caution you against its reception; and I would even venture to say, that at the present moment the balance of evidence is against the supposition that tubercle can be produced in animals by any of the means which I have specified.

For I may inform you in addition, that, not only in rabbits, but in sheep, and in cats or dogs which have been made the subjects of experiment, a very large proportion (I refrain from saying *all*) of the alleged tubercular deposits, artificially produced, prove, on careful examination, either to be instances of parasitic development in the substance of the lungs, or to consist of some other morbid product utterly unlike human tubercle.

One sort of experiment does apparently tend to develop tubercle. As we often stay the process of phthisis in the human subject by transferring our patient to a tropical climate; so, conversely, we can facilitate the development of the disease by importing the subject of our experiment from warmer to colder latitudes. It is said that, among the beasts in the Zoological Society's gardens, tubercle is a frequent cause of death; and especially among those which come to our climate from one of higher temperature. From my own knowledge, I will only venture to confirm this statement in regard of monkeys: as they have the dignity of standing next to man in form, so they have the inconvenience of this very human liability: when transferred from the hotter climates to England, and when surrounded by the artificial circumstances of a menagerie, they are apt to die with tubercles in their lungs, mesentery, and spleen.

The influence of temporary, or even habitual, deficiencies in air, in exercise, in diet, though it be insufficient to insure the production

of tubercle in those persons who are free from inherited disposition to the deposit, is yet quite sufficient to arouse all the energy of that disposition, if it be latent; or, in any man (whether with or without scrofulous predisposition) to excite an infinite number of those atrophic and inflammatory lesions which I have already generalized as apt to occur in depressed states of the system. And to the mention of these disorders I shall presently add that of another morbid condition, which is of easier artificial production than tubercle, and yet seems, in many respects, very nearly akin to it: I mean the fatty degeneration of certain tissues.

Here, however, let me detain you on the subject of the *hereditary transmission* of scrofula, and explain to you what I mean, when I speak of its being continued in this manner from generation to generation. I do not mean that, in the process of impregnation, actual tubercular matter passes from the system of the scrofulous father into the germ of the infant, to remain latent there, till circumstances call for its development; nor that, during uterine life, the blood of the child is poisoned by its mother's blood, as occurs in smallpox or syphilis. What I mean is this;—that the scrofulous diathesis—that the *disposition to form tubercles* is transmitted; that the child inherits an imperfect pattern of development.

I must explain this more fully, for the inheritance of *dispositions to disease* does not belong to scrofula only; it forms a very important problem in the pathogeny of cancer with its allied disorders (for they are often hereditary) of gout and rheumatism (for they, too, are heirlooms in families); and it accordingly constitutes one of the most considerable questions in the study of General Pathology.

Every one recognizes in the process of generation a certain amount of hereditariness—a certain amount of that influence by which a parent becomes the pattern of formation for his child. One allows for accidental deviations—for hare-lips, for club-feet, even for an occasional acephalism; but, these allowances being made, one prognosticates with great certainty as to the result of any particular sexual intercourse. No man expects to become the father of an armadillo, of a flying-fish, or a stag-beetle; nor (except in the Arabian Nights) do royal husbands believe that their princesses can be accouched of logs of wood. But, more than this, it is expected, and, on the whole, very generally realized, that the child shall be more like its father than its godfather. So far the case is clear; but I wish you to observe the tendency further. Follow the child in its ulterior development (for that is the point) and mark how exactly, in various exterior and noticeable signs, he repeats the development of his father; how, in arriving at the age when his father got corpulent, he acquires the same figure; how, at the age when his father became gray, or bald, he, too, becomes gray or bald, and with the same succession of parts—vertex first, or temples first, or forehead first, as the case may be; how his teeth decay, or drop, or protrude, just as his father's; how his pulse is of the same general character—even, as I have often noticed, to the degree of copying an intermittent rhythm (not accounted for by organic heart-

disease); and how his habits of sleeping and waking follow the same direction.

Now observe (for the distinction is of great importance) that these things are not *connate;* the child is not born a copy of his father as he begat him; but he is born, having his father's past development as a type for his own future development, so that he shall be developed as his father was developed, and shall hereafter become like him. In addition to that *general law* of human development, by virtue of which he is destined to be a mammal rather than a bird; and a man rather than an ox; and to reach puberty, manhood, old age, and death in a certain defined succession; he is further possessed by an inherited *personal and particular law* of development, which affixes a something peculiar and individual to his passage through each period of his existence.

If my meaning in all this has been intelligible to you, you will readily conceive that diseases *affecting the development of the body* are peculiarly those which would transmit themselves in the line of hereditary succession; that the disposition to a disease would be hereditary, where the disease consisted in the results of a faulty type of development, affecting limb or viscus, solid or fluid in the body; and that no disease would be hereditary except in so far as it might be developmental.

Practically, this is notorious. There used to be a comical print in the shop-windows, with the inscription "a chip of the old block;" it represented an old seaman having his infant son presented to him; and this new-born individual was made to carry the family-likeness by having a wooden leg exactly like his father's. Every one could smile at this absurdity, because of the general recognition of what I have just stated to you. Accidental mutilations do not become hereditary; for many centuries the Jews and the Mohammedans have undergone circumcision of the prepuce; but the local deformity has never transmitted itself; the new-born Jew or Mussulman offers probably as much foreskin to the knife, as the immediate successors of Abraham or Mohammed. If, on the contrary, one could so regulate the embryonic development of a human being, that it should be born having one leg, or no prepuce; and still more, if one could repeat this modification of development for two or three generations; then, I entertain no doubt that the peculiarity acquired in these generations would transmit itself indefinitely in the future productions of the race.

And, if you transfer these arguments to the several varieties of disease, you will know, on the one hand, in what diseases to anticipate hereditary transmission; and, on the other hand, what peculiar character of disease (to wit, its developmental character) may be inferred from the fact of its hereditary succession. Of a disease like scorbutus or ague, dependent on the presence or absence of certain exterior accidental conditions, you would anticipate that it could not be hereditary, any more than a wound or a dislocation. Of those accidental accompaniments of scrofula—the morbid processes which arise in defective nutrition (the ulcerations of the cornea

or intestines, for instance, which depend on insufficient or inappropriate nourishment) and which, as I have said, are essentially coextensive in their duration with the exterior causes which produce them—you would know that they could have no natural tendency to perpetuate themselves in this way. Of another disease, on the contrary—one like plethora, relating essentially to the rate or degree of development in an element of the body, you might predict that it would tend to become hereditary. And whereas it is in the blood, more strikingly and more constantly than in any ingredient of the organism, that development is ever in progress; whereas, it is eminently in the blood, that we have at each moment an epitome of the whole development of the body, and find the earliest rudiments and the latest relics of every organized tissue, nascent or in decay; so surely it would be in this fluid—the scene or the subject of so many developmental metamorphoses, that one would expect to find the material explanation of many hereditary diseases. One would expect that an inherited disposition to form, at various periods of life, and in a number of different organs, certain special and characteristic materials, bearing definite relation to the normal products of the body, would indicate a peculiarity in the development of the blood, whereof those deposited materials would be the result and the expression.

Such is the state of the case in regard of scrofula; and therefore it is, that I have analyzed this question of hereditary tendencies to disease. Strict experiment would not, I think, justify me in telling you *as a certainty*, that the scrofulous diathesis has its explanation in such grounds as we have gone over; but, though we are short of absolute demonstration on the subject, I may tell you this with confidence: there exist many facts rendering it highly probable that tubercle has its rise in disease of the blood; that this disease of the blood is one affecting its development; and that it is as a *developmental disease of the blood* that scrofula acquires its tendency to hereditary succession—its tendency to perpetuation as part of a family likeness. I shall presently give you other evidence in support of the same view.

Meanwhile, to return for a moment to the narrower ground from which we started, remember, that what is meant in calling scrofula an hereditary disease is—not that the tubercular material is to pass from parent to child—not that the child is to be born with tubercle already in its body, but that the disposition to *form blood in a manner which shall give tubercle as a collateral phenomenon*, exists as a clause in the child's charter of life, and forms a part of its type of development, as truly as any exterior resemblance which he may bear to the configurative growth of his parents.

I may illustrate to you the importance of these considerations, in quoting the result of some statistics collected at the Consumption Hospital, by the officers of that institution, and published by them in their last year's Report. They find that, among their female

phthisical patients,* thirty-six per cent. report their parents to have been consumptive. If you consider this statement simply, you will be struck with its importance, and with the magnitude of its consequences; and in order to do full justice to it, you must further remember, that, in the remaining sixty-four per cent., there may have been another considerable proportion whose parents had not, indeed, suffered from tubercular phthisis, but may have suffered from tubercular deposit predominantly in other organs than the lung—in the lymphatic system, perhaps, or elsewhere; and that there may have been a second considerable proportion, in whose family the parents may, perhaps, have escaped tubercular disease in their own persons, but may yet have transmitted the predisposition from their own immediate predecessors to those later inheritors of the disease: for it is notorious, in many matters of family likeness, that some very characteristic feature, healthy or morbid, may develop itself only in alternate generations, or may at least remain latent during a single generation, unless many circumstances conspire powerfully to favour its evolution.

With respect to the material of tubercle, you so often have opportunities of seeing it, that I need hardly detain you with any elaborate description of its characters. "When in that condition that its properties are most clearly marked, and when at that period of its development that no dissentient opinions are held as to its nature, it presents (says Dr. Walshe†) the following characters: "It is an opaque substance, of yellowish colour; sufficiently firm, yet friable; of little tenacity, and resembling cheese very nearly in point of consistence; inelastic; without particular smell; accumulated in small masses, varying in size from a pin's head to a hen's egg; of homogeneous aspect all over their divided surface; exhibiting no vessels; insoluble in water, and, if mixed therewith, quickly subsiding to the bottom. And these are the properties of a material which, in respect of its physiology, is characterized by its tendency to become soft, after it has existed for a variable period in the condition of firmness, and to induce various changes in the natural textures with which it is connected—changes eventually effecting its own complete disintegration and elimination. In the same natural texture with such tuberculous matter as we have now described are very frequently found certain small bodies, varying in size from that of a pin's head to a very small pea, of grayish-white or grayish tint, and glistening aspect. These bodies occur in different organs and textures, in association with yellow tubercle; they are more or less transparent; and though in their own substance of light-grayish colour, their translucency sometimes gives them, in appearance, the tint of the circumjacent structure; their section exhibits a smooth and close surface; hard as cartilage, almost, in some instances, and invariably remarkable for firmness;

* I dwell rather on the female patients, because, as is well observed in the Report, their closer domestication enables them usually to give better information than males can afford regarding the histories of their parents.

† Cyclopædia of Anatomy, vol. iv.

in general outline seeming roundish, yet in reality of somewhat angular form, and adhering so closely to the adjoining tissues, that they cannot be removed without particles of these; they have a striking tendency to accumulate in groups."

Such, then, gentlemen, are the two conditions in which the scrofulous product may show itself—either as the *yellow tubercle*, or as the *semi-transparent gray granulation;* and as regards the relations of these to each other, it appears that (in organs where both occur) the gray granulation is the earlier deposit; that it may be seen alone; that the yellow material may be seen in its substance and may gradually take its place; that, in short, it may fairly be considered to constitute a first stage of the local disease, and to be preparatory for the more characteristic yellow deposit. This, however, must not be understood, by any means, as of universal application; for there are many organs (as, for instance, the lymph-glands and brain) in which the gray granulation has rarely or never been seen, although the yellow tubercle is among their frequent diseases; so that the former deposit cannot be considered necessary for the development of the latter. It is especially in the lungs, that the gray granulation is habitually encountered; and in these organs unquestionably it seems to form a point of attraction—a matrix or a nucleus—for the yellow deposit.

The material of tubercle habitually presents itself in the shape from which its name is derived—namely, as *tubera* or rounded bodies, varying from the size of the smallest pin's head to that of an orange; evidently attaining their larger development by means of exterior accretion; and tending, where numbers exist together, to coalesce into irregular (though still tuberiform) masses. Where the individual tubercles have reached the size of the smallest pea, their substance consists almost invariably of the yellow material. In some organs, the structure which intervenes between separate tubercular masses, will show to the naked eye no other than its normal characters; but in the lung it is frequent to find considerable inflammatory condensation of this intervening tissue. Sometimes, too, in this organ, a large irregular extent of structure will have lost its natural sponginess, will have become dense and impervious to air, though still moist and compressible, and will present, on section, a nearly homogeneous, glistening, semi-transparent section, at various points of which one may perceive the deposit of yellow tubercular material. It is this latter condition—one by no means frequent in its occurrence—which is known by the name of tubercular infiltration; it apparently consists in the accidental presence of true tubercle in the midst of common chronic hepatization of the lung from pneumonia, and may be supposed to depend on a partial tubercular change of some prior inflammatory exudation.

Tubercular deposit in the lymphatic glands is in so far an exception to the general description I have given, as not to present itself at first in the spherical or tuberous form. Sections of a scrofulous lymph-gland, made when its mass is only partially tubercular, show

an irregular yellow blotting of the cut surface, not arranged in circles or segments of circles.

Masses of yellow material, like firm curd-cheese—existing either in a concreteness which allows it to be squeezed from the diseased organ as though from a follicle, or else diffused in the substance of such an organ, and blended with its structure, so as not to be insoluble by pressure or dissection; and smaller masses of semi-transparent gray material, extremely firm, and presenting a close resemblance to certain forms of fibrinous concretion observed on the valves of the heart; these, then, are the two sorts of deposit habitually noticed in the tissues of scrofulous persons; and it will be obvious to you that the first-mentioned is the characteristic and distinctive product.

Microscopical examination of tubercle shows the following principal ingredients: (1) a substance which constitutes distinctively the bulk of the gray granulations, and which in its general character is identical with the matter of condensed fibrinous concretion; namely, a dense, transparent, and almost homogeneous stroma, soluble in acetic acid and in the alkalies; (2) granular material, often in overwhelming abundance, especially in the yellow tubercle (where it is superadded to the former constituent) and consisting partly of fibriniform granules, partly of molecular oil; (3) aborted cytoblasts, dark, condensed, mis-shapen, angular, insoluble in acetic acid.

These, it appears to me, are the characteristic elements of tubercle; and, in addition to them, we habitually observe the admixture of other and accidental products—viz., (4) calcareous granules, frequent in some forms of tubercle, representing the material by which they are liable to cretaceous transformation, and consisting mainly of the phosphate and carbonate of lime; (5) shapes evincing the various stages of pus-development, and derived from inflammatory changes in the adjoining non-tuberculized parenchyma of the organ—changes due to the proximity of the tubercular concretion, and manifested chiefly at the period of its softening; (6) especially in the lung, a variety of cell-forms native to the organ; epithelium of larger and smaller bronchial tubes, ciliated and non-ciliated, often presenting partial abnormalities of growth due to chronic irritation of the mucous membrane; (7) blackening carbonaceous deposit, which is especially common about such gray granulations as are becoming obsolete; (8) plates of cholesterine and glomeruli of oil, mixed in the detritus of softened tubercle; (9) remnants of the original tissues through which the tubercular deposit has been infiltrated; as, for instance, in the lung, fragments of elastic fibre.

No formation of new bloodvessels ever occurs in connection with the processes of tubercular deposition. On the contrary, each mass, as it forms, effects a complete obliteration of all the capillaries within its sphere of infiltration, so as to become utterly non-vascular. In the concrescence of several tubercular masses, intermediate arteries and veins may remain pervious, and continue to maintain the circulation of blood in parts more distant; but the tubercle itself, however large, has no trace of capillary circulation in its interior; it is essentially bloodless.

You will observe, in this enumeration of the elements of tubercle, that I make mention of no characteristic cells. I know of none such. I believe that, so far as a given mass is tubercle, so far it is incapable of originating or maintaining any process of cell-growth; and I suspect that some observers have fallen into the error of describing, as characteristic of tubercle, cells which have been derived from the inflammation of adjoining textures. With exception of those large glomeruli or granuliferous cells, which are found in the fluid of softened tubercle (just as in deliquescent venous coagula) appurtenant to the disintegrating process, but neither characteristic of tubercle nor habitual to it at other periods of its existence—with exception of these (which are probably of extrinsic origin) and of the undoubted products of inflammation furnished by the vicinity, I am ignorant of any cell-growth associated with tubercle.

The aborted and stationary cytoblasts which I have mentioned, are very general in tubercle, and probably represent modified natural elements of the lymph and blood. I should hesitate to speak of them as invariably and diagnostically present, but I do not know that I have ever failed to see them. They are not particularly abundant in the gray granulation.

The ulterior changes of tubercular matter, when once it has been deposited in mass, are almost invariably in the direction of deliquescence. Exceptionally, the gray granulation may become horny, hard as a shot, and incapable of further intrinsic change; or the yellow mass may lose its animal ingredients, and become the seat of a permanent calcification; but, speaking generally, tubercle tends to soften by some chemical conversion of its material, and thus in a liquefied form, to be discharged from the system by the ulceration of surrounding parts. It is this process, long confounded with suppuration, with which you are familiar in the process of phthisis, as leading to the formation of vomicæ, and as continuing in an infinite majority of cases, to form cavity after cavity in the lung, till the patient sinks exhausted, by their discharge and irritation. It is the same process, again, which leads to the formation of scrofulous abscesses in the lymph-glands of the neck or mesentery, and in other organs of the body; where we have opportunities of observing the curative processes (identical with the healing of ordinary abscesses) which ensue in parts not of vital importance, when the tubercular material has been enabled to discharge itself.

In the progress of softening, the stroma of the tubercle vanishes; the molecular oil and other molecular matters increase; the involved elements of natural tissue break up, and add the products of their disintegration; serum and pus are contributed by the surrounding structures; glomeruli arise; and the whole mass, becoming saturated with fluid, shows, on microscopical examination, a mixture of organic detritus with incidental inflammatory products.

When this change has commenced, the circumjacent parts probably contribute to its completion, by furnishing an additional fluid which favours the decomposition of the tubercle; but the change is originated, as an intrinsic and characteristic one, in the tubercular

material itself; commonly commencing in the interior of its concretion, where the product is of oldest formation, and where the influence of neighbouring tissues would of necessity be least. Its resemblance to the well known softening of fibrinous coagula in veins is too remarkable to be overlooked—a resemblance both in the steps of the process and in its material results. This is rendered the more interesting from the obvious similarity which exists between tubercular matter and fibrin, in respect of most chemical characters and of some general physical qualities. There seems no reason to doubt that these processes are essentially identical, and that the pathological gist of scrofula consists in the deposition and ulterior deliquescence of a fibriniform material.

The often-asked question—Is tubercle an inflammatory product? seems to be answered in anticipation by the description I have already given you. In itself, it is clearly no product of inflammation, but is apt, especially at the period of its softening, to act as an irritant of surrounding textures, and to invite the addition of their inflammatory exudations. The evidence of its non-inflammatory origin—the evidence of its origin as a concretion—seems sufficiently furnished by the results of microscopical examination; and to this may be added the testimony of all clinical observers, that tubercular accumulations may advance latently, and may reach considerable magnitude or extensive diffusion, without producing in the patient any signs, local or general, of inflammatory action. It is important, however, to know that its mechanical interference with the circulation of blood is great. In the lungs—for some reason hitherto unexplained—this obstruction to the passage of blood acts peculiarly, and leads to the occurrence of hæmoptysis. We do not find hemorrhage habitually associated with tubercle in other organs of the body; nor do we find that other than tubercular deposits in the lung readily induce hemorrhage there; but this particular deposit in that particular organ produces the result with extreme frequency. In the first Report of the Consumption Hospital, it is stated that about two-thirds of their phthisical patients suffered from hæmoptysis; and in nearly three-fourths of this number the symptom in question arose *before* the occurrence of softening; when, namely, it must have depended on the rupture of bloodvessels from their mechanical obstruction, and not on their being opened by any ulcerative process.

I have now to state to you the *order of preference* in which different organs are invaded by tubercular disease; and I may take this opportunity of saying explicitly (if I have not already done so) that I look upon the scrofulous deposit, which we so often find in the glands of the neck and in other lymphatic glands, as identical with the material of pulmonary and other visceral tubercles. Both chemical and anatomical examinations establish this view, in my opinion, so conclusively, that I am quite unable to understand how it is that some pathologists still hesitate to admit the fact. The description which I have given of yellow tubercle, as it occurs in

the lung, would apply with equal accuracy to scrofulous deposit in any other organ of the body.

As respects the choice of organs for scrofulous deposit, I can give you infinitely better authority than my own, in quoting the observations of Professor Rokitansky; his pathological statistics—founded, as they are, on what he well calls "colossal materials," can be equalled from no other source. The annual necropsies in the General Hospital at Vienna probably exceed at least twenty-fold those which occur yearly in any one of our large London hospitals; and Rokitansky's great name has been connected with this unique school of pathology, I believe, during twenty years. In summing up figures for such statistical deductions as I am about to give you, his materials must consist of more than *tens of thousands* of instances. The following, then, on his authority, I give you as the order of frequency with which different organs are found tubercular in the dead body: Lung; intestinal canal; lymph-glands, especially the abdominal and bronchial; larynx; serous membranes, especially peritoneum and pleura; pia mater; brain; spleen; kidneys; liver; bone and periosteum; uterus and Fallopian tubes; testicle and its appendages; spinal marrow; voluntary muscles: and, in children, this order of precedence so far undergoes a modification, that the lymph-glands and spleen stand first in the list.

But, in order to be rendered a true transcript of Nature, this list requires a very important qualification. It confounds together the primary tubercular deposits with those which have occurred as secondary formations, during the fatal progress of the disease; counting, for instance, tubercular ulceration of the intestines as an unit for the statistical table, whensoever it is found in the dead body, although perhaps it may never have been discovered, except as a posterior complication of other tubercular disease. The important question obviously is this—by what organ does scrofula first possess itself of the system? not—what organs are oftenest found tubercular in *post-mortem* examinations, where several organs are simultaneously seen to be diseased? but—what organs are selected by Nature for the first invasion of the disease?—what organs give the greatest facilities for its characteristic deposit? Hear Rokitansky again: The lungs and the lymph-glands still maintain, in a very high degree, their numerical superiority to all other organs affected singly; while the intestines, larynx, and trachea, serous membranes, spleen, and liver, fall at once from the high level at which they stood in the less discriminative list; they fall so low as to indicate, conclusively, that they are almost, or quite, insusceptible of the primary invasion of tubercular deposit;—that they suffer only in a secondary way, and are visited (so to speak) only by the superfluities of the disease.

This is matter of immense importance. The organs, in which the disposition to primary deposit almost exclusively prevails, are such as may, with equal exclusiveness, be called the *organs of blood-development;* and in this generalization we possess a clue, which it

is impossible to over-estimate, for arriving at a true interpretation of this fatal disease.

We have next to inquire, respecting the several organs in which tubercle occurs—what anatomical relation is borne by the morbid deposit to the natural tissues of the organ.

In the lymph-glands, I suspect that tubercle is in truth no *deposit;* that it is not derived from the blood in the vessels there ramifying, but is an accumulation in the tubes of the gland of their own morbidly coagulable or inspissated lymph; that it is therefore not, strictly speaking, a disease of the lymph-gland, but of the lymph in the glands.

As respects other organs, it seems that the readiness with which the tubercular material coagulates prevents its passing to any distance from the vessels which have furnished it. Accordingly, we do not find it occurring in tissues which derive their nourishment by imbibition through some length of extra-vascular structure, as cartilage. But in organs which consist of involuted mucous membrane, with a more or less solid plexus of bloodvessels, we find that the deposit readily concretes on the free surface of the membrane; thus, in the lungs, it may be seen to lie as a secretion in the air-cells, till it has collected in sufficient quantities to obliterate their septa, and microscopically to appear as what may be termed tubercular infiltration. Among the observations which illustrate the first deposit of tubercle in the lung, I have much pleasure in citing those of my colleague, Mr. Rainey; and I recommend you to read attentively the paper on this subject, which he communicated to the Medico-Chirurgical Society in 1845. In other compound mucous organs I have seen the same thing; for instance, in the follicles of the uterus, and in those of the vermiform appendage; while a mash of softened tubercle has been lying over the general surface of the mucous membrane, I have been able to isolate the subjacent follicles, to see them full of apparently tubercular matter, and yet with their definite limitary membrane quite uninjured. However, while I entertain not the slightest doubt that tubercular matter concretes readily within the air-cells, on the free surface of the limitary membrane (for on many occasions I have seen it occupying this position) I should hesitate to admit that this is its exclusive seat, even in the earliest commencement of the disease. In studying injected specimens* of pulmonary tubercle, one sees many nebulæ of deposit, which show no trace of subdivision according to the arrangement of air-cells, and which yet do not appear of sufficient density to have caused the destruction

* Among the most important specimens illustrating the deposit and increase of tubercular matter in the lung, I must mention those prepared by Mr. John Quekett for the College of Surgeons, of whose Museum he is the Assistant-Conservator. By his labours, during the last few years, this great collection has been rendered so rich in microscopical specimens of healthy and morbid histology, as to have become an invaluable museum of reference to all persons engaged in such pursuits. Every one availing himself of its resources must concur in a feeling of obligation—not only to Mr. Quekett's large knowledge of his subject, but to the cordial readiness and good-nature with which this knowledge is at all times rendered auxiliary to the scientific objects of those who visit the collection.

of membranous septa. I am not able to tell you with certainty, whether the tubercular element of the blood may coagulate within the capillary vessels of the lung, and in their immediate proximity; but there are pathological reasons for considering this as not improbable, and as helping perhaps to explain the extreme power of obstruction which tubercle exercises on those vessels, and the singular tendency which it possesses, beyond all morbid interferences with the pulmonary circulation, to produce the symptom of hæmoptysis.

Likewise, among anatomical peculiarities of this deposit may be mentioned, that in almost every organ there is a favourite spot, where the masses of tubercle first appear. Thus, in the lungs, there is the well-known preference for the summit; in the pia mater, for the region of the base, about the commencement of the optic nerve and the fissure of Sylvius; in the brain itself, for the gray substance; in the osseous system, for the cancellated structure; in the bowels, for the lowest part of the ileum; in the testicle, for the epididymis; in the female sexual system, for the Fallopian tubes and fundus of the uterus.

Next we have to inquire—What are the pathological affinities of tubercle? what diseases does it refuse to coexist with? with what diseases is it often associated?

First, for the negatives: Rokitansky, whose immense materials are again a sure resource, says: Tubercle hardly ever occurs in those who are the subjects of cystic tumours, such as those of the ovary: Bronchocele seems incompatible with it, and ague is alleged to be so: it is with the utmost rarity that tubercular patients are attacked with typhus. Tubercle and cancer are incompatible.

Lastly, I told you in a former lecture, that Rokitansky attaches great importance to an increased *venosity* of the blood, as an antagonistic condition to the formation of tubercle; and under this head he includes every influence which interferes directly or indirectly with oxygenization of the blood, either by diminishing the capacity of the chest, or hindering the expansion of the lungs, or by deranging the pulmonary circulation of blood, or by impeding the free access of air thereunto.

For example: a case of spinal deformity narrowing the chest; a case of abdominal tumour encroaching upward, and causing dyspnœa; a case of cyanosis maintaining deficient aeration of the blood; these would be cases in which, according to this observer of hundreds of thousands, the tubercular deposit would not arise.

With respect to those contrary classes of disease, with which tubercle most readily associates itself; there stand, first of all, those atrophic, ulcerative, and sub-inflammatory processes, to which I have already adverted as apt to occur in depressed states of the system, and which maintain (as I explained at the commencement of my lecture) only an accidental affinity to tubercle. But there is one very important class of structural changes, which the tubercular constitution so habitually associates with itself that I can hardly refrain from considering their mutual relations important or essential. I allude to what is called the fatty degeneration of the liver,

the kidney, and the arteries; and I am disposed to believe that, when our knowledge of the subject has become more complete than it now is, we shall find proof that these fatty degenerations stand in some essential relation to the tubercle-forming diathesis—stand perhaps in the relation of secondary dependence on it. You will rarely make the *post-mortem* examination of a tubercular patient without finding an augmented formation of fat in one, two, or all of the three situations I have mentioned; in the liver, constituting its well-known fatty enlargement; in the kidney, associated with those other changes which concur with it to constitute the scrofulous form of Bright's disease; in the arteries effecting their atheromatous degeneration, weakening their coats, and disposing them to aneurism or to rupture. In the liver, this fatty deposition occurs as a very simple change, merely increasing (though often to an immense extent) that molecular oily ingredient, which is native to the endothelium of the gland, and which is visible microscopically in the form of minute globules of oil within the limits of each nucleated cell. In the artery, other changes are associated with the fatty accumulation—at least, whenever it is extreme; changes which have suggested to pathologists a suspicion that the atheromatous degeneration consists in the fatty conversion of some fibrinous or fibriniform material previously deposited there. In the kidney, likewise, at least in that of the human subject, the process of fatty accumulation (shown, as you look on the section of the gland, by a vast number of bran-like spots diffused usually over a pale and flabby surface) is far from being a simple one: you never see the kidney extensively affected in this way, without observing simultaneously that there exists some considerable destruction of tubules, or some serous or fibrinous infiltration of the gland, for which the presence of fat in its endothelium would be insufficient to account. That fatty accumulation in the kidney, confined to its endothelium, and existing there as a primary deposit, constitutes the proximate cause of the scrofulous form of Bright's disease, is a view which I cannot consider supported by conclusive evidence. Many of the microscopical forms (some derived from the tubules during life, others from sections of the organ after death) which have been ascribed to fatty engorgement of the endothelium, are indistinguishable from the *glomeruli* which arise in fibrinous and bloody effusions, and which (as in the white substance of the brain) are often met with in parts not naturally possessing a nucleated cell-growth.

In the domestic cat—at least in our metropolitan cats—the tubules of the kidney almost invariably (though I presume abnormally) contain a very large quantity of oil; and I think it probable that this quantity may artificially be increased by interference with the locomotion and respiration of the animal. This is a condition of simple fatty accumulation, analogous probably to the fatty liver of the human subject. Though immeasurably greater in degree than any similar accumulation ever observed in the human kidney, it is attended by no destruction of the tubules; nor does it often, if ever, interfere with the function of the organ or with the health of the

animal. Some years ago, too hastily, I believed that these kidneys were exquisite analogies of our scrofulous form of Bright's disease, and would explain its human pathology; but further investigation has convinced me of the inaccuracy of this first impression.

Let me now, gentlemen, in a few paragraphs, collect for you the total result of our present knowledge of tubercle, and state to you what inferences may be drawn as to its true pathology from those extensive generalizations which I have set before you.

The material products of the scrofulous diathesis consist in some mis-developed proteinous ingredient of the lymph and blood. The essence of this mis-development lies in the fibriniform solidification and concretion of something which should remain fluid in the plasma of the blood. I call it *fibriniform*, because—though it is not identical with fibrin, it probably arises in some analogous method of formation, and undergoes similar final metamorphoses. This solidification occurs in the ascensive development of the lymph and blood: it occurs with an infinite preference in the lymph-glands and in the lungs; in the former, where lymph is brought into intimate relations with arterial blood; in the latter, where lymph (which is constantly accruing to the blood) first comes into immediate relations with the atmosphere. It seems, then, to affect the total blood, only by reason of the lymph which is contained in it; in other words, not to be a disease of the total blood, but one of the lymph or nascent blood. Precipitability by the atmosphere is the characteristic of this morbid product; its places of election are determined by this peculiarity: tubercles form, where lymph and blood get their first opportunities of increased oxidation. In accordance with this law, venosity of the blood precludes the tendency to tubercular deposition. The fibriniform product of scrofula is insusceptible of development: it is a dead concretion. Like true fibrin, it may become the seat of calcareous deposit, and may thus form a permanent inorganic concretion. Like true fibrin, it chiefly tends to soften, and its softened substance is copiously infiltrated with fat: probably it undergoes a fatty degeneration. The diathesis in which tubercular deposits occur, is accompanied by a remarkable tendency to the accumulation of fat in the liver, and to the fatty degeneration—either of the substance of other organs, or of some previous infiltration in those organs: possibly this tendency may indicate that the fibriniform material of tubercle in its molecular state can undergo, either in the blood, or in those organs, the same degenerative changes as affect it in its concrete condition. In short, the scrofulous diathesis consists in an inherited peculiarity of blood-development, under the influence of which the nascent blood tends to a molecular death by super-oxidation; partly it may appear that these dead proteinous elements can undergo, within the stream of the circulation, such degenerative changes as will qualify them for discharge by excreting organs; partly it may appear that these changes lead to fatty accumulations in the endothelium or in the parenchymatous blastema of such organs; but mainly and characteristically, it is the way of those dead proteinous elements to concrete in the organs where their

precipitation has been determined, and there to construct the fibriniform masses called *tubercle*. These masses undergo changes of deliquescence and destruction, which tend to their ultimate expulsion from the system, but which, as they entail the disorganization of all surrounding textures by inflammatory and ulcerative processes, are commonly defeated in this tendency when they occur in vital organs (as the lung) or attain it by the complete sacrifice of the invaded organ, as when present in lymph-glands, testicle, or breast.

I have told you that cancer and tubercle are incompatible diseases—that the one excludes the other. You cannot wonder at this. They are pathological antitheses in regard of the blood. In the one case, if I may use so strong a phrase, the blood dies stillborn; it never attains its maturity of growth or function; it stops short of the distributive arteries of the body; it never reaches the aorta; it perishes and decays on the threshold of the circulation. In the contrary case of cancer, there is an obstinate excess of vitality, which will not be quenched. You remember how the blood's plasma, as though out of a luxuriance of life, contributed—not to perishable concretions, but to profuse living growths; you remember how these growths, tending to an effort of elimination, still maintained an uninterrupted dependence on the blood, constituting the strange paradox of an organized excretion; you remember how they evolved themselves with exhaustive rapidity out of a too fructifying blastema, vegetating without limit at the expense of other organs, till the whole fluid of the circulation seems to devote itself, away from its slower and legitimate uses, to this impetuous by-play of organization.

Our therapeutical knowledge of tubercle is scanty in the extreme. We are not sure that we possess a drug capable of interfering with its deposit. Iron, which acts so powerfully on the corpuscular development of the blood, and which must therefore, in some degree, affect its total progressive changes, has acquired no reputation for the prevention of tubercular concretions. Cod-liver oil, which is said to influence materially the earlier stages of blood-development, has latterly been much vaunted as a contra-scrofulous remedy; its credit, in many cases, is well deserved, and its alleged action on the blood would seem to bring its method of operation nearer to the root of the disease; but much in all this is conjectural, and I dare only speak of it as a matter for continued observation, whether the drug does really affect the initiative acts of blood-development, and whether it does really counteract the tendency to tubercular precipitation. Of the iodide of potassium we know nothing at all; and we have only some very crude and general analogies to guide us to an impression, that its action would rather consist in disintegrating and removing the morbid product, than in hindering its first formation.

Climate, as I have already told you, is a most material influence for and against the development of tubercle. A degree of scrofulous diathesis, which would tuberculize the lungs of a patient in England, would leave him quite unscathed in Cairo, or at the Cape; and, conversely, a minor degree of the diathesis, which would be harmless in

a tropical climate, would determine the development of phthisis, if its subject should be made an inmate of our colder atmosphere. I cannot refrain from connecting these notorious facts with that which I have already told you, as to the anti-tubercular power of an increased venosity of the blood. The first and most essential change, wrought by the transference of an animal from England to India, is in the respiratory function, and, consequently, in the oxidation of the blood. Where the thermometer stands at 90°, the quantity of respiration (owing to rarefaction of the air) must be very much less than where the thermometer stands at 45°; the blood will, consequently, be in a condition of relative venosity, and the disposition to tubercular precipitation will be *pro tanto* diminished. This, I have no doubt, is the manner in which transference to a warmer climate acts beneficially in the *prevention* of tubercular disease. More than this—where the deposits already exist, or where the ulterior destructive changes have commenced in them, a warm and equal atmosphere can exert a palliative tendency, in diminishing the liability to those catarrhal complications which are so frequent in our precarious climate. Do not believe, in regard of your scrofulous patients, that climate will prevent the softening of tubercular masses which already exist, or that it will insure the cicatrization of cavities already formed, or about to be formed. Its power is much more limited than this: it will counteract very powerfully the disposition to further deposits; it will give Nature more chance of effecting the discharge of softened tubercle in her own gradual manner than if the process were to be complicated with constant renewals of catarrhal inflammation; and in both these respects—provided there be no large extent of vital organs diseased—it will give powerful assistance towards the patient's recovery.

LECTURE X.

Nervous Symptoms. Generalization of normal nervous phenomena, and of their respective relations to anatomical divisions of the nervous system. Physical morbid phenomena: (1) Anæsthesia, (2) Subjective sensations, (3) Paralysis, (4) Involuntary movements. Mental morbid phenomena. Causes of abnormal excitement or depression in central organs; humoral, sympathetic. Sympathies: (1) co-ordinate; homogeneous or augmentative; heterogeneous or reflex; (2) ascensive and descensive. Therapeutical control over nervous centres; cold; belladonna; strychnine; tobacco; chloroform; opium.

Gentlemen: In to-day's lecture, I wish to consider with you so much of the pathology of the nervous system as relates to the analysis and interpretation of symptoms arising in that system. In order to investigate such symptoms with success, you must be well informed in those great physiological results which have been increasing yearly, by the labours of all the chief anatomists of Europe, since the publication of Bell's discovery. For a complete summary, and a very just appreciation of those labours, I cannot do better than refer you to the articles published in the *Cyclopædia of Anatomy*, by Dr. Todd, who has himself likewise contributed largely to the elucidation of this difficult subject, and especially to the various chemical applications of nervous physiology.

In a few paragraphs I may give you those generalizations, on which hitherto we chiefly rely for our analysis of nervous symptoms.

We recognize the nervous system as the sole seat of all organic changes immediately relative to the consciousness of the individual —relative (that is) to his several acts or attitudes of sensation or effort, of appetite, sentiment or passion, of judgment, imagination or will. We recognize it likewise, as the sole seat of all those intermediatory influences (independent of consciousness) which, in the living body, regulate the actions of contractile tissue, according to impressions primarily made on other tissues; as, for instance, when the iris (without our knowledge or wish) modifies its pupillary opening in consequence of a certain impression made on the skin, the cornea, or the retina.

Anatomically, we discriminate the constituents of the nervous system, as *gray* nerve-matter, and *white* nerve-matter; the latter essentially consisting of *tubular* elements; the former of *vesicular* elements; the latter essentially constituting *nerve-cords*, the former essentially distinguishing the *nerve-centres* or ganglia.

Physiologically, we recognize that aggregations of gray nerve-matter are the true and specific centres of nervous function; that *to them converge* the results of exterior impression; that *from them emanate* the immediate influences which determine motion; that they are *terminal* in respect of impression; *dynamical* and originative in respect of motion. We recognize that the nerve-cords are mere

channels of communication; intermediatory either between the nerve-centre and some impressible surface which affects it; or between the nerve-centre and some contractile tissue which it affects; or commissural between it and co-ordinate nerve-centres; or between it and super-ordinate and sub-ordinate nerve-centres.

For in every developed nervous system we observe a gradation in the centres of function, according to the extent of their influence. First, there is the *supreme* dynamical centre, which is susceptible of changes immediately and necessarily associated with the consciousness of the individual, and which more or less directly influences all other centres; this probably comprehends only the convolutionary surface of the cerebrum. Next, in at least two gradations, come the *subordinate* cerebro-spinal centres, which are only mediately associated with consciousness: (1) *a lower grade of centres*, including the special centres of individual parts, whether the material of those centres be discrete (as on sensitive nerves and in the sympathetic system) or be massed into continuous columns (as in the interior of the spinal cord); (2) a *higher grade* (including the gray matter of the cerebellum, of the optic thalami, and of the corpora striata) which are the centres apparently of aggregative action, standing in a first degree of subordination to the centre of consciousness, and serving intermediately to collect the impressions and regulate the phenomena of those several special centres which are subordinate to them.

The lowest nerve-centre has for its simple function to receive the notice of impressions, and to react on that notice. As the stage and mechanism of its operation, the following anatomical arrangements are necessary: a surface which may receive exterior *impressions;* an organ which may *contract* on stimulation; an *afferent nerve* which may convey to the centre the exterior impression; an *efferent nerve* which may convey from the centre to the contractile organ, that specific stimulus on which it is the latter's function to contract.

To this apparatus the whole phenomena of the nerve-centre may restrict themselves: the exterior impression, conveyed to the centre and stimulating it, may excite reaction, which reflects itself to the contractile tissue, evincing itself there in the result of motion; and thus the effect may terminate.

In the human subject (to which for obvious reasons I confine myself) it is only among parts supplied exclusively or chiefly by the sympathetic system that the subordinate centres habitually and normally act in independence of higher centres: the contractions of the heart and arteries, of the stomach and intestines, of the bronchial and Fallopian tubes, neither require that a sensation should precede, or an effort of will determine them; nor are they determinable by any voluntary effort. We shall presently see that this capacity for independent acts, which normally belongs as a habit only to the nerve-centres of vegetative life, exists as a latent function in the subordinate cerebro-spinal centres likewise, and is apt to show itself in them (in the form of characteristic reflex phenomena) chiefly when the influence of the higher centres is withdrawn.

In health, however, while the several segments of the nervous system fulfil their appointed functions, an impression made on any surface innervated by the cerebro-spinal axis commonly excites no reaction from those subordinate centres which lie between the impressed surface and the centre of consciousness; it is only on the latter—the supreme centre—that its effect is produced; and there it is recognized as a *sensation*. Similarly, the movements which arise in any contractile textures under cerebro-spinal influence, do not commonly depend on the unconscious reaction of subordinate centres, primarily exerted; but depend on the energy of the highest centre, transmitted to the muscles through those subordinate centres. in the form of a *volition*.

The only partial exception to that rule lies in regard of certain instinctive movements, which (in all the voluntary muscles, but especially in those of respiration) are apt to occur for preservative and defensive purposes, without the previous occurrence of a distinct volition. I call it a partial exception, because such movements, though they often or usually occur in an involuntary or semi-voluntary form, are yet within the distinct cognizance of the individual, are matters of sensation to him, and are controllable by his will. Of such movements you have familiar examples in the instantaneous retraction of a hand or foot that has unexpectedly encountered a sharpness—in the sudden closure of the eyelids as anything darts before them—in the convulsive cough which follows irritation of the glottis—and, indeed, in the ordinary actions of inspiration; since we can, at any moment, in our own persons, substitute deliberate voluntary breathing for that semi-conscious, semi-voluntary process by which we habitually respire. It seems certain that the dynamical source of these instinctive actions lies in those accumulations of gray nerve-matter, which extend on either side, from just above the decussation of the pyramids to the floor of the lateral ventricle; which have the ganglionic centres of the higher senses and of respiration ranged around and blended with them; and which themselves (as I have said) may be considered as aggregative centres of sensible impression and motional reaction—habitually subject to the higher control of the centre of consciousness, but capable under certain circumstances of determining and maintaining definite automatic movements without the intervention and authority of that higher centre. These cerebral sub-centres of instinctive and emotional action apparently include the corpora striata, optic thalami, and those continuations of their gray nerve-matter, which extend into the medulla oblongata, under the name of *fasciculus innominatus*, (*faisceau innominé* of Cruveilhier. Acting in the abeyance of the higher centre, they are capable of exciting the several subordinate centres of the cerebro-spinal system to determinate actions; acting in union with (or rather in subordination to) the high centre, they are intermediate to the production of conscious phenomena—namely, to the inward transit of a sensation, to the outward transit of a will.

Co-ordinate with these centres in the double relations just indicated—sub-ordinate (that is to say) to the centre of consciousness,

and super-ordinate to the spinal centres, is the third cerebral sub-centre, the *cerebellum ;* having apparently for its function to balance and harmonize those various muscular exertions of the entire body, by which, in station, progression, and athletic efforts, we unconsciously turn to the best account the mechanical endowments of our frame; a function, which is intimately associated with our impressions of *direction* in space—with our sense of downward, upward, forward, backward, sideward—and which seems, in its ordinary performance, to occur as an ever-fluctuating muscular equilibrium, graduated and proportioned in its several component forces, by distributive modifications of muscular tone, which are themselves reflex to impressions conveyed to the sensorium, perhaps through various channels, but specially and distinctively through the semicircular canals of the ear.*

In order to save repetition, and remove ambiguity from my analysis of an intricate subject, let me tell you here the sense in which I shall employ certain words in the course of this lecture, and in which I would advise you to employ them. By "primary centre," or "centre of consciousness," or any equivalent phrase, I mean the gray nerve-matter of the convolutions of the cerebrum. By "secondary centres," or "centres of aggregation," I mean the cerebellum, the optic thalami, the corpora striata: the second and third of these I may occasionally call "cerebral sub-centres;" and as it is in the highest degree probable, though perhaps not yet quite susceptible of logical demonstration, that the optic thalamus is the aggregative centre of sensation, and the corpus striatum of voluntary motion, so I shall speak of them as the centres of these functions respectively, without, in each case, qualifying the phrase with some adverb of uncertainty. Remember, however, that though there is no doubt as to their joint functions as aggregative centres of sense and motion, their separate share in respect of these functions is not yet irrefragably demonstrated. In speaking of these sub-centres, too, I include under their name the gray nerve-matter which prolongs them backwards as far as the medulla oblongata. By "tertiary centres" I should imply the special cerebro-spinal centres of indi-

* It was Professor Wheatstone's ingenious conjecture, that the semicircular canals—standing always in planes rectangular to each other, and corresponding, therefore, to the three axes of solidity, would be accurate acoustic measures of the direction of sound. That they bear a definite relation to the function of the cerebellum seems a conclusion inseparable from the experiments of M. Flourens, who found that lesions of the semicircular canals produced the same in co-ordinate movements as arise from injury of the cerebellum, and that the convulsive efforts of motion which thus arise with lesion of the semicircular canals, vary according to the canal injured, just as with lesion of the different crura cerebelli: that uncontrollable forward-motion will have attended the injury of one canal or one crus; uncontrollable motion backward will have attended the injury of a different canal or a different crus; uncontrollable motion of rotation will have attended the injury of a third canal or a third crus. From these very important experiments, it would be difficult to deduce any other inference than that conveyed in the text, that the semicircular canals furnish recipient surfaces for impressions of direction in space, and that these impressions excite the cerebellum to the production of reflex phenomena, which are normally confined to the maintenance of bodily equilibrium and the co ordination of voluntary movement, by means of commensurate gradations of muscular tone.

vidual parts: namely (1) the gray nerve-matter of the spinal cord (which consists of innumerable special centres massed together in vertical columns); (2) the ganglia of sensitive nerves, which are discrete; and (3) those centres of special senses and special movements, which exist about the mesencephalon, and which (for convenience of package, and perhaps for readier intercourse) are grouped closely about the aggregative centres, and blended with their surface; so that while there is every physiological evidence of their distinctness, we are not able to effect an anatomical separation between them; such, for instance, is the relation of the visual centres (corpora geniculata and quadrigemina) to the thalamus, misnamed *opticus*. By "quaternary centres" I mean those of the so-called sympathetic system of nerves; and as I shall often have occasion to use the words *sympathy* and *sympathetic* in relation to the sense of "concurrent function," it will save obscurity if I avoid applying the same words to the nerve-apparatus of organic life, and I shall therefore speak of that apparatus throughout as the "ganglionic" nervous system. By "sensation" and "will" I uniformly imply *consciousness* of some objective change, or of some subjective effort: by "impression" and "motional reaction," I imply the analogous incidence of objective change, or effluence of motional stimulus, without any affection of the consciousness. By "receptivity" I mean that function of a nervous centre by which it receives and is susceptible of impressions. By "reactivity" I mean that function of a nervous centre by which it tends to excite the phenomena of muscular contraction. By "peripheral surface," in relation to sensitive nerves, I mean that tegumentary or other surface on which exterior impressions first impinge—a surface occupied by the elementary distribution of the nerve.

It will be obvious to you from what I have already said, that, in the simplest apparatus of innervation associated with the organs of consciousness, there lies the possibility of disease under either of the following forms: viz., (1) a distal impression may fail to produce its proportionate central sensation; (2) a central sensation may exist without a proportionate distal impression having been made; (3) a central volition (or the stimulation equivalent to it) may fail to excite its proportionate muscular contraction; (4) muscular contraction may exist in parts normally under the influence of the will, without the previous occurrence of a volition, or of any equivalent stimulus.

(1.) *Anæsthesia* is the name given to the first form of disease—that in which the patient remains without cognizance of impressions made on a surface normally sentient. It is not only in respect of the cutaneous surface and the function of touch, that this may occur. The same condition may affect other organs of sense: the visual apparatus, giving amaurosis as its result; the auditory, causing deafness; the olfactory and gustatory, producing interruption of their functions. Such disease may depend on a variety of causes. The peripheral *surface* originally impressed may be incapable of its function, by reason of some disorganizing process which has invaded its nervous expansion, or by reason of inflammatory products which

are pressing there. Such are the cases of amaurosis which arise in over-use of the eye, with congestion of the choroid, and slow disorganization of the retina; or cases of deafness, in which the vestibular expansion of the *portio mollis* has been destroyed; or cases in which loss of smell has arisen from the progress of ulceration or inflammatory thickening in the upper passages of the nose; and, in considering such instances, be careful to distinguish them from others, where the sentient surface is uninjured, and where the interference with its function is indirect and exterior; such, for example, as where blindness depends on opacity or malformation of the optical media—on cataract or leucoma, on too great or too little convexity of cornea, and the like; or where deafness depends on obstruction of the auditory passages, or other disease in parts which are preliminary to the true acoustic apparatus. Cases of the latter sort obviously do not belong to the class of *nervous* affections, any more than that comparative insensibility of the cutaneous surface which may be caused by horny thickening of the epidermis; the nervous expansion is healthy, but is rendered inaccessible to moderate impressions. Disease in the *convective apparatus* and in the tertiary nervous centres may interfere with the transmission of impressions, and constitute the cause of anæsthesia; as we see where some special nerve has been cut asunder by accident or intention, or has been disorganized by disease, or has undergone compression by a tumour; or where disease or injury of the spinal cord interrupts the continuity of impressions from the circumference of the nervous system to the centre of consciousness. It is in one or other of these ways, that local anæsthesia of the cutaneous and mucous surfaces commonly arises, and sometimes the failure of the higher senses: we have illustrations of this, when disease in the trunk of the fifth nerve, or in its Casserian ganglion causes semi-facial insensibility, and partial loss of taste; when encephaloid growths in the optic nerve, or irregular osseous tumours about the foramina of the sphenoid bone, cause blindness; when softening of the spinal cord, or pressure on it by the deformity of vertebral disease or injury, leave the lower limbs and the bladder insensible to contact. Disease in the *cerebral sub-centre* of sensation (the optic thalamus and the gray nerve-matter adjoining it) is the common cause of hemiplegic anæsthesia; more common by far, and of more direct operation, than disease in the convoluted surface of the hemispheres, which we recognize as the centre of consciousness. Apoplectic clots, chronic inflammation, atrophic softening, especially the first two, are the anatomical conditions which are most commonly associated with this symptom; and as these aggregative centres of function represent the sensations of the side of the body opposite to their own, we find that the hemiplegic anæsthesia which their disease induces, is on the side opposite to the lesion.

(2.) The consciousness of a sensation without the precurrence of a distal impression, constituting a phenomenon of so-called *subjective sensation*, may occur as a symptom of nerve-disease, under influences inferior in activity, though similar in kind, to those which produce

anæsthesia. Sensations arising in disease of the peripheral surface cannot, strictly speaking, be considered subjective phenomena; seeing that, in such instances, an impression equivalent to the sensation is really produced at the distal extremity of the nerve. Flashes of light conveyed to the patient's consciousness by the irritation of a congested choroid telling on the retina; *muscæ volitantes* produced by minute particles floating in the transparent fluid media of the eye; buzzing in the ear from over-vascularity of the mucous membrane of the tympanum; these are evidently not subjective phenomena, because (though their immediate causes do certainly lie within the body) they depend in each case on distinct objective changes, affecting the distal extremity of the nerve, and producing sensation only equivalent to those changes. True subjective sensations arise in disorders of the convective apparatus of innervation, and in disorders of the subordinate centres; depending for their production on this law—that incident nerve-tubules are incapable of conveying to the centre of consciousness any other presentation than that of the surface whence they originate; so that, whether they be normally affected in the peripheral surface where they rise, or abnormally in any intermediate part of their course; or whether their special centres be affected, or the cerebral sub-centre of aggregation to which they finally tend; in any case, the subject can become conscious only of such sensations as would be produced by impressions at the distant peripheral surface where the nerve-tubules arise. Thus it is, that in hitting the ulnar nerve at the elbow, we have the sensation of an injury to the inner fingers; thus, that pressure on the sciatic nerve at the buttock produces a sensation of "pins and needles" in the foot; thus, that the inflamed nerve of a stump conveys to the patient's mind so distinct a sensation of the amputated extremity, that he can hardly dissuade himself from the conviction that he still has fingers or toes there, paining him. Affections of the subordinate nervous centres act similarly: a tumour of the spinal dura mater pressing slightly on the cord, or idiopathic softening of this organ (before either disease has advanced sufficiently to cause paraplegic anæsthesia) will produce subjective sensation, imitative of impressions made at the feet and legs: a tumour of the Casserian ganglion will produce sensations which the patient confidently refers to the nervous expansion on his face. It is in these diseases of sub-ordinate centres—chiefly of tertiary centres—that *neuralgia* so commonly arises; for by this term, when it is properly used, we denote the subjective experience of pain in a part where there is no equivalent objective disease; and in most of such cases the disease is not in nerve-tubules, but amid the gray nerve-matter of the secondary or tertiary centre. Partial disease in the optic thalamus, no less than disease of the Casserian ganglion, may cause to the patient's consciousness the impression of agonizing pain in the several cutaneous branches of the fifth nerve: no less than disease of the spinal cord, it may originate impressions of formication, of pins and needles, and the like, in the extremities—differing, however, from the spinal disease in producing its symptoms hemiplegically instead of paraple-

gically; and, no less than disease of the optic nerve or corpus geniculatum, it may cause sensations referable to the eye, sparks, and blazes of light, &c.

In all these various cases, the subjective sensation will be the characteristic one of that nervous expansion to which the impression is referred; if the affected nerve or centre be one of cutaneous innervation, the patient's feeling will be of some variation in exterior contact or temperature; if the nerve or centre of vision be affected, the result on his consciousness will be that of luminous objects, flashing, blazing, or sparkling before him; if the nerve or centre of hearing be disordered, the abnormal sensation will be one of sound, grating, rumbling, creaking, or crashing beside him; if the gustatory nerve or centre be affected, the subjective impression is (or has been where I have witnessed the symptom) relative only to the tactile function of the tongue: the patient has a constant uneasiness (equivalent to formication in the skin) which suggests to him that his mouth is full of hairs or grit.

Subjective sensation, either in the severest form of neuralgia, or in some slighter manifestation, may exist without any discoverable organic disease; and it is practically of great importance, as a point conducing to accurate diagnosis, to notice whether the neuralgic affection be, or be not, accompanied by anæsthesia. Attention to this point will often enable us to give confident prognosis as to the issue of a particular case, by determining whether the symptoms are such as to imply destructive disease in the nervous apparatus of the part. Neuralgia of long duration can hardly exist separately from anæsthesia, as a result of such disease; and if we find it continued for a long period in this simple form, we may pretty confidently predict its non-dependence on permanent organic lesion.

(3.) Of *muscular paralysis*—the third symptom in our list—you probably know many illustrations. When a muscular nerve has been cut or compressed, or when some similar disorganizing influence has operated on the nervous centres of motion, the latter become incapable of originating, the former of conveying, the efficient stimulus of muscular contraction; the muscles remain unaffected by the will and by other circumstances which would naturally determine their action. You may see the iris reduced to this condition from disease of the third nerve; so that, although light enter the eye largely, and be felt acutely by the patient, the pupil remains uncontracted in size. You may see a similar state of things in half the face, when some swelling about the parotid gland has compressed the portio dura after its exit from the skull, and has rendered it incapable of conveying to the muscles any stimulation, voluntary or reflex, arising in their special nervous centre. You observe the same symptom affecting the lower half of the body, when a fracture of the spine, or its chronic curvature, or primary disease in the spinal marrow, has cut off the lower part of its axis of tertiary centres from the influence of the brain. And you are familiar with the same paralytic condition, as it affects one vertical half of the body, in consequence of disease directly or indirectly operating on the

corpus striatum. I may take this opportunity of mentioning to you, that hemiplegia and paraplegia are seldom exclusively confined either to sensation or to motion; it is chiefly the more partial nerve-diseases, involving some separate nerve-cord, which thus restrict themselves; for although in the tertiary spinal centres a certain quantity of gray nerve-matter corresponds undoubtedly to motion, and a certain other quantity to sensation, and although similarly in the brain the thalamus opticus and the corpus striatum appear equally distinct in their aggregative functions, yet in both cases (and especially in the spinal cord) the proximity of these sensitive and motional organs to one another is such that the structure of one can rarely be much affected without disturbing the function of its neighbour.*

(4.) Contraction in voluntary muscles, excited without the influence of volition, sometimes occurs partially in a single muscle, or set of muscles; sometimes is more or less universal, and constitutes the character of so-called *convulsive* diseases. Occasionally, but rarely, you may see involuntary muscular contraction, arising in some disease or injury of the convective apparatus: the cramps of the lower extremities which arise during pregnancy are of this nature. And sometimes one observes permanent contraction of a muscle associated with injury of the nerve-cord supplying it: I have seen the flexor muscles of the inner fingers thus contracted, after laceration of the ulnar nerve at the elbow. Partial organic disease of the spinal cord, and pressure on it by tumours, or by displaced bone, are very common causes of muscular cramps in the parts below the seat of lesion. Sometimes, too, there will be hemiplegic rigidity of muscle, occasioned in the same manner as hemiplegic paralysis, by apoplexy, inflammation, or atrophy in the opposite corpus striatum. The muscular cramps which precede a paroxysm of gout probably indicate an irritation of the spinal centres by vitiated blood. But the most extensive development of involuntary muscular contraction occurs usually without the pretext of demonstrable organic disease, and arises in mere functional excitement of the motional centres of the nervous system. Such are the irregular twitching and jerking movements of chorea, the sustained rigidity and recurrent spasms of tetanus, and the struggling paroxysm of epilepsy. With respect to the portions of the nervous system primarily affected in these disorders, it is difficult to speak with certainty, because of their

* I do not wish to imply, in these or other phrases of my lecture, that I consider the spinal cord in any respect a central organ of *impression*. Unquestionably it contains the tertiary centres of *motion*, as well as the tubules by which these centres are maintained in dependence on their super-ordinate centres of aggregation within the cranium; but, as respects *impression*, it is far from improbable that the ganglia of the posterior roots may be the only tertiary centres of this function, and that the cord itself may contain no gray nerve-matter subservient to sensation, but merely tubular nerve-matter commissural between those extra spinal ganglia and between them and the thalami optici. Pending the uncertainty, one may include the ganglia of the posterior roots under the head of *spinal centres*, and consider them as co-ordinate with those tertiary centres of motion which form the bulk of the gray nerve-matter within the cord. Throughout this lecture, wherever I speak of the spinal system or spinal axis, generally, I include these discrete ganglia just as though they formed part of its substance.

merely functional nature; but the following appear probable conclusions: (1.) That *tetanus* belongs essentially to the tertiary centres of the spinal cord and medulla oblongata, not including (so far as one can isolate their respective functions) the aggregative centre of motion (the corpus striatum) and certainly not the centre of consciousness. (2.) *Chorea* certainly is not an affection of the spinal centres primarily; as is shown, in part, by the frequency with which it is hemiplegic; in part by its frequent origination from mental causes, which operate on the primary centre; in part, by the quiet given to its characteristic movements under the influence of sleep, when the function of the higher centres is in abeyance, and when physiology teaches us that the special functions of the tertiary centres would be rather exalted than depressed. That it is not disorder of the convoluted surface, seems likewise certain, from the non-affection of consciousness, even in the severest cases of the complaint; that it is an affection of a secondary centre, seems little less than certain; namely, either of the aggregative centre of motion (corpus striatum) or of the organ which co-ordinates the voluntary movements (cerebellum); in the present state of our knowledge, it would be rash to offer an opinion as to which of these sub-centres is the primary seat of the disease; but—that the motional centres of the spinal cord are affected only secondarily, by means of their superordinate centre, seems the natural explanation of the symptoms. (3.) In the paroxysm of *epilepsy*, there is more complication; the symptoms clearly imply that more than a single centre is involved —at least, in the perfect fit; on the one hand, consciousness is arrested, which implies an affection of the convoluted surface of the cerebrum; on the other hand, general clonic convulsions occur, which imply the excitement of some aggregative centre of motion; but here (as with chorea) it seems impossible at present to pronounce whether the cerebellum plays the important part in producing these convulsive movements, or whether they depend on excitement of the corpus striatum. The affection of the primary centre appears the essential thing in epilepsy, for the failure of consciousness is characteristic, and may exist (in the form which the French call *petit mal*) without involving the occurrence of convulsions; while the latter never exist without the former. The intellectual changes which precede, accompany, or follow the progress of the disease, its concurrence with insanity, and its tendency to dementia, further mark the convoluted surface of the hemispheres as the primary seat of the morbid process.

Such are the primary symptoms, which the organs of innervation are liable to furnish; namely—pain; insensibility; paralysis; convulsion. And, before leaving the subject, I may briefly remark to you, that it is not only in respect of bodily phenomena that you may thus analyze symptoms derived from the nervous system. The changes relative to consciousness—the changes in the mental phenomena, are similarly reducible to method. The type of mental function in the nervous system is like that of physical function; intellectual *perception* and moral *will* representing, in this higher sphere

of operation, those functions of *receptivity* and *reaction*, which we have observed in the lowest nervous centre, under the respectively analogous forms of *incident impression*, and *reflected motional excitement.* In the centre of consciousness (the hemispherical surfaces of the cerebrum) morbid changes may arise strictly analogous to those we have considered in the subordinate centres; there may exist an anæsthetic condition of the mental receptivity, or an unreactive state of will, so that no cognizance is taken of the several sensations which are aggregated in the cerebral sub-centres; and no other movements are performed than those instinctive ones which are irrespective of consciousness. Such a state it is which we witness in the extremity of idiocy or cretinism. Or there may exist a hyperæsthetic condition, in which the patient's consciousness is embarrassed by false presentations, illusions, phantasms, dreams; a condition in which he is haunted by *spectra* analogous to those visual and auditory sensations which arise in connection with disease in the optic or acoustic nerve; a condition in which the centre of consciousness, abnormally excited, forges subjectively all manner of images of incident and circumstance, with a self-assurance of their objective reality, just like that which a neuralgic patient entertains as to the outwardness of his central* pain: this form of insanity is well illustrated in the access of delirium tremens, and in the healthy brain may be partially imitated by the action of opium. Or there may exist a condition of exaggerated impulse, in which (either with or without, but usually with, this excitement of the mental receptivity) there arise uncontrollable caprices of will, objectless endeavours and exertions; varying from the transient intoxication produced by laughing-gas to the permanent forms of the so-called moral insanity; and constituting as extreme a distortion of the patient's normal spontaneity, as tetanus or epileptic convulsion constitute of his voluntary muscular contractions. But on these subjects it is impossible for me to dwell further than to remind you, that delirium and coma are our daily illustrations of these twofold aberrations; the former representing the excitement, the latter the oppression, of the centre of consciousness; and that, in watching these attentively, you will have many opportunities of learning the relations which subsist in disease between the receptive and the reactive functions of the mind; and between these conjoint functions of consciousness, and those subordinate functions of physical life, to which I have more particularly confined your attention.

From a consideration of the above symptoms, you will observe that they resolve themselves, pathologically, into two heads: (1) there may be *interference with nervous connection*, due to an affection

* This state of mind is well depicted in Byron's Dream:—

"She was become
The queen of a fantastic realm; her thoughts
Were combinations of disjointed things;
And forms, impalpable and unperceived
Of others' sight, familiar were to hers."

of the white nerve matter, and usually dependent on some mechanical lesion of a nerve-cord or of the spinal marrow; or (2) there may be *central disease*, manifested either in depression or in excitement of the function of the affected centre.

The first class of causes does not at present require further mention from me; but it is important that you should carefully consider the circumstances under which *nervous centres* become liable to excitement or depression.

I. Where exaltation of function is evinced by the cerebro-spinal centres, as a primary nervous phenomenon, or where any primary variation tends to transientness and periodical recurrence, it may be inferred, with high probability, that the origin of such disorder consists in some influence of which the blood is the vehicle — that the nervous symptom is one of humoral causation. The delirium and coma which arise from alcohol or opium, and the spinal excitement which is caused by strychnine, are illustrations of the operation of contaminated blood on the nervous centres. Central neuralgia arises with the utmost frequency in anæmiated and debilitated persons. Often, again, we observe it and other forms of subjective sensation, arising in patients either notoriously the subjects of gout, or in whom we have every reason to suspect the latency of that diathesis. Chorea confines its attack to individuals in whom the blood development is obviously defective: it is so commonly associated with disordered intestinal excretions, that purgatives have acquired a celebrity in its treatment; and it unquestionably has some close affinity with that condition of system which leads to the occurrence of rheumatic fever. Epilepsy has a peculiar disposition to occur in persons whose secretion of urine is materially deranged, and its tendency to periodical occurrence is one which strongly suggests its dependence on specific materials accumulating in the blood. You know how often epilepsy attends the termination of Bright's disease; and that phenomena accurately resembling it, have been produced (under similar circumstances) in the lower animals, whose kidneys have been experimentally removed. Epileptic fits are apt to be severe in proportion to the intervals between them, which is a further confirmation of the same view; and sometimes the paroxysm will be deferred to a period when the morbid influence has gathered to such intensity, that when at length the requisite momentum is given to the fit, its severity is so great that the patient perishes in its access. My friend Dr. Todd (in his admirable Lumleian Lectures,* to which I am indebted for much valuable information on the subjects we are now considering) suggests very plausibly, that the cases of sudden death from so-called *congestive apoplexy* are really of an epileptic nature, arising in the manner here intimated; and he proposes for such attacks, with great propriety, the name of "epileptic coma."

Of persistent functional disorders of the nervous system, it appears that a large majority arise in conditions of defective or dis-

* On Convulsions, Delirium, and Coma; published in the *Medical Gazette* for 1849 & 1850.

ordered nutrition, affecting the secondary and tertiary centres—conditions which are primarily unattended by structural lesion, but which, under injudicious treatment, readily advance to that atrophic state which we know as white softening of the nervous substance. It is matter of daily observation, how readily and uniformly these diseases give way to general tonic treatment, and especially to that medicine which favours the progressive development of the blood, namely, iron.

As regards the affinity between cholera and rheumatic fever, it does not by any means appear to me that the humoral disorder is identical for the two diseases, since they are never coincident in their occurrence; but it seems, rather, that the material which collects in the blood prior to the attack of rheumatic fever, and which, by its explosive decomposition, subsequently evolves the immense evacuations of this disease, may, while accumulating within the circulation in its original form, become capable of producing that irritation of the nervous centres which is characteristic of chorea.

II. In other, and very important instances, the phenomena of nervous excitement or depression arise in a secondary, and so-called *sympathetic* manner, which is quite peculiar to the nervous system, and is essentially unattended by structural disease;—namely, by the propagation of functional change, perhaps in an exaggerated form, either from one nerve-cord to another by the intermedium of a nervous centre, or from one centre to another by continuity of nervous substance.

It is extremely important for your understanding of nervous symptoms, that you should know the forms in which nervous sympathy is apt to show itself.*

Some of the best instances of such sympathy are afforded in the movements of the iris. Why should the pupil become smaller, by contraction of the iris, whenever the internal rectus muscle turns the eye inwards? or when light falls on the retina? or when the cornea and conjunctiva are irritated? why should it at once become larger when the opposite eye is covered with the hand? or when belladonna is applied over the tegumentary distribution of the fifth nerve?

In analyzing sympathetic phenomena furnished by the cerebrospinal system, you will find it convenient to consider them, first as they occur between co-ordinate centres (*co-ordinate sympathies*); next as they occur between subordinate and superordinate centres (*ascensive or descensive sympathies*); an din each instance to distinguish whether the sympathy consists in an increase of the original

* An admirable analysis of nervous sympathies is furnished by Professor Henle in his recently published *Handbuch der rationellen Pathologie.* His earlier exposition of the same subject was given in a separate volume of Essays (*Pathologische Untersuchungen;* Berlin, 1840), and was digested for the English reader in Dr. Forbes's Quarterly Review. Dr. Marshall Hall's well-known investigations, and those of Magendie, Mayo, Brachet, Mueller, Grainger, Valentin. Bidder and Volkmann, Stilling, Henle, Koelliker, Budge, Wagner, and Weber, have contributed in various proportions to swell the mass of material, which Henle and Stilling especially have endeavoured to systematize.

sensation, or original motion, as the case may be (*augmentative sympathies*), or consists in a translation or reflexion of that original influence, so that motion is generated by an incident impression, or sensation arises dependently on the excitement of motion (*reflex sympathies.*)

I. *Co-ordinate sympathies* would be such as exist between the cerebral sub-centres, or between those several tertiary centres which are massed together in the spinal cord, or are ranged about it. When the pain of a whitlow (which first of all was confined to the immediate vicinity of the nail, where alone the inflammation exists) presently includes the finger, then affects the whole hand, then the forearm, and finally gives uneasiness to the whole extremity as high as the shoulder, the only rational explanation of this diffused pain is —that the tertiary nervous centre corresponding to the inflamed spot, being vehemently irritated, propagates its excitement to the co-ordinate centres of impression nearest adjoining it, causes to the patient's consciousness whatever impressions of pain these adjoining centres can originate, and thus produces the subjective *spectrum* of a more extensive disease than really exists. In this case the diffusion of excitement is confined to centres of the same degree, and is homogeneous in its nature—the original pain producing further pain; and the seat of this excitement is apparently the gray nerve-matter of the spinal system—only in its sensitive portion, and only on that side of the body where the original irritant prevails. Recently, I visited a gentleman who was suffering severely with what is called muscular rheumatism in a very small portion of the deltoid; there was intense tenderness in a space not larger than a crown; every attempt at voluntary exertion of the muscle was accompanied by extreme pain; and at the moment of its chief severity this discomfort did not confine itself to the affected muscle, but extended through the whole extremity from the scapula to the hand, and diffused itself so extensively that, even up to the neck and down to the leg of the same side of the body, a dull heavy pain was simultaneously experienced. This is another illustration, just like the last, of *augmentative* sympathy of *sensation* arising in the propagation of excitement *unilaterally* among *homogeneous* and *co-ordinate* nerve-centres. The pain referred to the knee, in case of disease in the hip-joint; the semifacial, semicranial, and at last semicervical pains, which often develop themselves out of a simple toothache, are similar illustrations of nervous sympathy in co-ordinate centres. The pains produced in the right shoulder, by inflammation of the liver, in the left shoulder by disease of the heart, and in the penis by calculus of the bladder, are doubtful illustrations of the same thing, because of the mixture of ganglionic influence in the innervation of these organs. Sometimes we can trace the vertical propagation of excitement along the sensitive axis of gray nerve-matter chiefly by means of reflex phenomena to which it gives rise. If our nerve-centres of vision are strongly stimulated by a dazzling glare of sunshine, their excitement diffuses itself to the adjoining centre of common sensi-

bility where the fifth nerve implants itself, produces a subjective sensation of tickling in the nose, and deceives Nature into the unnecessary effort of a fit of sneezing.

Sometimes excitement diffuses itself in a manner essentially similar to this but with one trifling difference: instead of propagating itself vertically in the cerebro-spinal axis, so as to involve an unilateral plurality of centres, it does so transversely; affecting the correspondent gray nerve-matter on the opposite side of the median plane, and giving rise to a subjective sensation of disease symmetrical with that which really exists. Ollivier gives the case of a patient in whom a wound of the spinal cord in the cervical region had rendered the left leg, and the corresponding half of the trunk below this injury, almost entirely insensible to contact: but when the integument of this left leg was pinched, the patient had a sensation at the corresponding spot of the opposite and healthy limb; the local impression had stimulated its special tertiary centre; this centre (owing to the injury) could not convey its intelligence to the centre of consciousness; but the excitement, diffusing itself transversely by commissural fibres, affected the adjoining and similar centre of the right side, and produced the subjective image of contact on that limb. In the same manner of transverse diffusion of excitement, it apparently arises that patients so often refer pain to a tooth exactly opposite to that which is carious, and which is the real cause of their suffering. We are also able to trace, in an opposite direction, the tendency of symmetrical nerve-centres to transfer and equalize their depression as well as their excitement; for (as I have already mentioned without explaining it) when you lessen the stimulation of one retina by covering the eye, the opposite pupil immediately opens wider, as though the stimulus had been directly withdrawn from *its* nervous centre: an effect which really depends on the contra-stimulant influence of darkness being diffused transversely from one visual nerve-centre to the other.

Motion as well as sensation, admits of sympathetic increase by unilateral and symmetrical spread of excitement among co-ordinate centres. In various cases of paralysis, where the spinal centres of motion are unaffected, we can find illustrations of this exactly equivalent to those which I quoted to you of sympathetic sensation. According to Stilling, if the spinal cord (in cats or frogs) be cut on one side as far as the median plane, so that the lower limb on that side shall derive no direct influence from the brain, not the less does it follow exactly the movements of the opposite limb. Magendie has observed a similar result in dogs; and in hemiplegic patients it is not unusual to observe unconscious movements of a paralyzed limb during the act of some emotional or instinctive exertion, in which the opposite healthy limb takes part; such, for instance, as yawning. Obviously, in all these cases, the phenomenon depends on the fact, that the spinal centres of the healthy side, deriving excitement from the brain, diffuse it to their adjoining fellows, so that the movement becomes symmetrical, as it would have been during health. And during the respiratory movements of hemiplegic patients, we

can frequently see similar evidence of vertical propagation of excitement in the motor axis of thecord; an excessive respiratory exertion, coughing, sneezing, and the like, tending to produce irregular movements in the paralyzed extremities; which (as they are not imitative of similar movements on the opposite side of the body) cannot be considered the results of transverse or symmetrical sympathy, but must arise in the diffusion of excitement, vertically, from the stimulated tertiary centres of respiratory movement. In tetanus, there is the utmost possible excitement of the motor axis of the spinal cord on both sides of the body; but as the symptoms of this disease (where it is traumatic) do not necessarily begin as muscular contractions in the wounded limb, gradually involving more and more of it, then more and more of its fellow, then more and more of the trunk, other extremities, and head;—as I see no traces in its history of this successive propagation, I apprehend that we have no sufficient reason for referring its origin simply to the influence of nervous sympathy.

Thus far, of what I have called *homogeneous* or *augmentative* sympathies among the co-ordinate centres of sense and motion respectively; but modifications of excitement in either of these functions may produce, as I have told you, *heterogeneous* or *reflex* phenomena. Of subjective sensation, sympathetic with motion, there are not many good examples to be found. There are of course very many instances of pain attending excessive muscular contraction, or following muscular fatigue; but in most of these it seems probable that the pain is objective—it is commonly referred to the disordered muscles, and seems to have a sufficient cause in their condition, without any need for supposing that it depends on a continuance of excitement from their over-active motor centre to some adjoining sensitive centre. Henle states (on the authority of Stromeyer) that after the division of tendons, when the muscle falls from a state of tension and spasm into one of perfect repose, it is common to find the skin over it, and sometimes to a considerable extent in its neighbourhood, become numb and partially insensible, and continue so till the tendon has reunited; when it will gradually recover its normal sensibility, with some amount of that formication which I have already mentioned to you as a subjective phenomenon of sensation. Perhaps the severe pain felt along the spine of the back after some sudden and violent act of coughing, or after any irregular contraction of the œsophagus; perhaps, too, the well-known stitch in the side after running; the tickling in the throat after long speaking; and cases of increase in facial neuralgia by muscular exertion—may be subjective phenomena dependent on the translation of excitement from a motor to a sensitive centre. A gentleman at present under my treatment for chronic irritation of the spinal cord (probably of gouty origin) does not constantly suffer much sensation of pricking in the integuments of the lower extremity, but any muscular exertion in the way of walking brings on this symptom in a very marked degree. Here, obviously, the primary excitement (associated with muscular exercise) must have its seat in the anterior

columns of the cord; and the subjective skin-sensation which ensues must depend on diffusion of that excitement to the posterior nerve-centres.

Of the translation of excitement in the opposite direction of the cerebro-spinal axis—namely, from the posterior to the anterior centres—giving rise to the phenomena of reflex motion, we have innumerable illustrations. The ordinary movements of the iris, in proportion to impressions of light on the retina, or of contact on the conjunctiva and skin; the closure of the glottis when it is irritated by foreign bodies; the constriction of the bronchi when pungent vapours assail them; the screwing up of the sphincter when we would pass an instrument through the anus—are familiar instances of this action normally exerted. It is peculiarly in parts that derive a part or the whole of their nervous supply from the ganglionic system—in the heart and arteries, and the hollow viscera of the abdomen—that this form of reflex action habitually prevails, as the simplest possible method of muscular innervation. When the tertiary centres of the cerebro-spinal system are withdrawn from the influence of the cerebral centres, they become capable of displaying this action to a degree not habitual to them while in their normal state. If by disease in the human subject, or by experiment in the lower animals, the spinal marrow be divided from the brain, or the aggregative centres of the latter organ be destroyed on one side, or on both, the limbs (which are then morbidly removed from the influence of consciousness and volition) become liable to reflex movements. Thus, for instance, in a hemiplegic patient, if you tickle the sole of the foot, though this impression be quite unfelt by the subject, it excites the receptive centres of the cord; these propagate the stimulus at once to the motor column, and involuntary movements immediately arise in the limb.* It is apparently as reflex phenomena that the spasms of tetanus arise: the disease consists (so far as we know) in an excessive functional excitement and tension of the nerve-centres of motion; their disposition to react on sensitive impressions is immeasurably greater than in health; a breath of air throws the unhappy patient into frightful agonies of convulsion. Dr. Mayer has shown, in respect of the very similar condition which may be artificially produced by strychnine, that if, in frogs thus poisoned, the posterior roots of the spinal nerves be cut partially or entirely, the tetanic condition ceases for so many of the muscles as are thus relieved from the possibility of reflex excitement. He can in this way (cutting all the posterior roots) entirely suspend the phenomena of tetanus; and can then only succeed in re-exciting their manifestation, by dashing the frog's whole body violently against some object, which may give concussion enough to the spinal cord to stimulate the ordinary impressions of exterior contact.

* The motional excitement thus produced sometimes diffuses itself extensively in its own column, and with a disproportion to the original impression that seems to show an almost tetanic irritability in that column. Henle quotes the case of an apoplectic patient, in whom strong sunlight produced violent and universal muscular spasms: it is rare to see the tertiary centre of vision become the medium of such sympathies.

It is probable that sympathies of this same nature exist between the co-ordinate sub-centres of the brain, and evince themselves especially in sudden apoplectic seizures; for though we have abundant reason to believe that the aggregative centres of sense and motion are distinct and separate, yet it is rare for hemiplegia—especially for sudden hemiplegia, to affect one only of those functions, leaving the other unharmed; and the joint affection of both functions, by a lesion affecting the centre of either one, would indicate such a sympathy as that in question.

Between the quaternary centres of the ganglionic system we can often trace the sympathetic diffusion of excitement. Henle gives a simple illustration of this in respect of the intestinal canal: the annular constriction of an exposed bowel, which may be brought about by mechanical irritation, confines itself to the immediate vicinity of the irritated spot, if the bowel be detached from the mesentery; but diffuses itself along the intestine, in the form of peristaltic movements (by reaction from co-ordinate nervous centres), if the natural connections of the part be unsevered. Though vomiting be not an act simply of the stomach, yet its ready occurrence during the passage of renal calculi, and under various other conditions of irritations or injury in the genito-urinary apparatus, points to sympathetic relations between the special ganglia of the stomach and those of the latter organs. The extraordinary variations in the action of the heart, under the operation of gastric causes—the palpitations and intermissions of pulse which a little flatus at the cardia will produce—and the sedative influence exerted over the circulation by the sudden impression of cold on the stomach—are illustrations of similar sympathies diffused from the abdominal to the thoracic centres of the ganglionic system.

II. Of sympathies between superordinate and subordinate nervous centres (*ascensive* or *descensive* sympathies) the chief instances relate to the mutual influences of the ganglionic and cerebro-spinal systems; but still there are some examples which are confined to the latter exclusively.

The insensibility—usually transient—which attends any considerable injury to the cerebral sub-centres (though they are not in any immediate sense the organs of consciousness) must be considered an illustration of *ascensive* sympathy operating, from these sub-centres (thalamus opticus and corpus striatum) on the higher centres of the hemispherical surface. Perhaps the delirium of irritative fever after injuries—the so-called traumatic delirium—may be another instance of the same kind. In epilepsy (unless we are to consider that in that disease the several centres are coincidently affected) there would be evidence of a similar sympathy; and, as the sudden affection of consciousness appears to be the essential feature of this disease, being both prior to the convulsions in each attack, and likewise more universal in its occurrence, one would conjecture that the sympathy must be *descensive*, operating from the centre of con-

sciousness downward on the aggregate centres of motion. We see a further illustration of this descensive sympathy in the paralyzing effects of mental emotion; under the influence of which our voices falter, our hands shake, and our knees bend tremulously under us. In sudden encephalic apoplexy, this same sympathetic depression of the spinal centres prevents them at first from responding to sensible impressions by the way of reflex motion; and it is only after a variable interval that they become capable of developing this characteristic phenomenon.

The propagation of functional excitement from the ganglionic system to the various cerebro-spinal centres, or from these centres to the ganglionic system, is a matter of notoriety. Sometimes the excitement diffuses itself *eodem genere*, or (as I have called it) augmentatively; sometimes the result is heterogeneous from the original excitement, or reflex. We see *motional* excitement propagated *descensively*, in that acceleration of the heart's action which is caused invariably by exercise of the voluntary muscles, and which can only be ascribed to the influence of cerebro-spinal excitement on the ganglia of the heart. We see it propagated *ascensively*, from the ganglionic to the cerebro-spinal system, in the phenomena of puerperal convulsions, which (if they occur during the process of delivery) associate themselves distinctly with the uterine pains, even under the influence of chloroform. Of sensational excitement propagated ascensively from the sympathetic to the cerebro-spinal centres, we see examples in that cutaneous itching that accompanies many mucous irritations; such as the itching of the nose from intestinal worms. I have known severe epigastric itching associated with chronic gastritis; and have removed an inveterate pruritus of the perineum by curing a stricture of the urethra. The vertigo which rapidly ensues in many persons from the ingestion of certain indigestible articles of diet; the intense brow-ache which often comes on at the moment when ice enters the stomach; the pain about the ribs and intercostal spaces, which is often associated with chronic disorder of the colon, are probably further illustrations of the same method of communication.

Impressions made on parts under the control of the ganglionic system habitually receive a direct response from the ganglia to which the stimulus of those impressions has been conveyed: thus it is that the heart, the bowels, the uterus, the arteries, sustain the muscular contractions which are essential to their vital uses. But there is some reciprocity of reflex function between the cerebro-spinal and the sympathetic systems; so that an impression made on the one may circuitously excite motory phenomena in the other. On the one hand, we see changes relative to sensation and perception produce the excitement of contractile tissue under the influence of visceral ganglia; see how emotion affects the heart, or how disgusting physical objects will cause almost instantaneous vomiting, or how the embarrassment of the senses in sea-sickness produces the same effect. Again, in speaking of the process of inflammation, I have shown some reasons for believing that the changes which occur

in the capacity of arteries, going to inflaming or overgrowing parts, consist in a reflex relaxation of their muscular coats: and as the afferent nerves in all cases of exterior inflammation belong to the cerebro-spinal system, the subsequent affection of the contractile tissue of the artery may probably be induced through a spinal centre, exciting the quaternary ganglion by which the artery is innervated. On the other hand we have opportunities of observing that impressions insensibly made on surfaces supplied by the ganglionic system, may induce reflex contraction in muscles supplied by spinal nerves.

A year ago I was hastily summoned into the country to visit a gentleman whose state was exciting some alarm; he presented the curious symptom of clonic muscular contraction on one side of his abdomen, recurring at intervals with extreme violence, and with such rapid alternations of spasm and repose, that during the paroxysm it presented the appearance of a large pulsating tumour on the right side of his abdomen: each access was accompanied with much pain. After very careful inquiry, I could discover no plausible explanation of this symptom beyond an unhealthy condition of the bowel over which these broad abdominal muscles were spread: there was reason to believe that the ascending colon was in a state of irritation from accumulated contents; and under treatment founded on this supposition the spasmodic attacks ceased and never returned. A more frequent and familiar instance to the same effect is the spasm of the cremaster (causing retraction of the testicle) which accompanies the impaction of a calculus in the ureter; and the involuntary consent of the abdominal muscles in the production of vomiting—whether in this case or in those of primary gastric derangement, must partially receive its explanation in the same ascensive diffusion and reflexion of ganglionic excitement.

Our therapeutical control over the excitement of nervous centres is hitherto imperfect; less for want of powerful agents than because of our want of precise knowledge as to their distinctive effects. The so-called sedatives, acting through the blood on the higher nervous centres, almost always commence their operation by stimulating those centres; and the so-called stimulants almost always produce a subsequent sedative effect; so that it is not easy to determine whether these two classes of medicine can be separated. Our management of central excitement may be illustrated in the following particulars.

By *cold*, directly applied, we can lower almost indefinitely the excitement of the centre, and can reduce it to a condition in which it will no longer furnish its customary reactions, whether healthy or morbid. Thus I have seen the application of ice to the spine, in hydrophobia, so depress the irritability of the cord as to remove all reflex convulsion from the effort of deglutition, and enable the patient to swallow with facility: but the heart's action was simultaneously so much reduced, that the sufferer very nearly died under the immediate impression of the intended remedy.* In tetanus, likewise, this remedy appears to have been used with advantage, as the means of directly depressing the motional excitement of the spinal centres.

* The patient eventually died.

It is probable that the influence of cold consists in its power of reducing the amount of organic change in parts of the living body, and that consequently it would be exerted with equal efficiency over any nervous centres to which refrigeration could reach.

There is another method of operation by which cold can depress nervous activity, and this method it has in common with many other agents—I mean its sedative influence on the peripheral nervous expansion. It is thus that ice taken into the stomach diminishes, in many cases, an extreme disposition to vomit; and that, by sympathetic extension of its influence, it likewise reduces an excited action of the heart. In neitheri nstance could the effect arise, except through depression of excitement in the nervous centre.

The action of *belladonna* on the iris (according to its common method of use in ophthalmic surgery) illustrates even better than the distal operation of cold, this indirect control over nervous centres. An anæsthetic agent operating on the peripheral expansion of the fifth nerve produces the *negation of excitement* in its centre; this condition diffuses itself to the motional centre of the iris, and as excitement would have shown itself in contraction of the pupil, so the opposite nervous condition evinces itself in expansion of that aperture. Where the reactivity of the spinal cord is very highly excited, a peripheral surface may, by the influence of belladonna, be rendered incapable of provoking reflex movements. Thus, for instance, if a frog be rendered tetanic by opium or strychnine, any contact of its cutaneous surface will produce universal spasm; if either before this poisoning or subsequent to its manifestations, one limb of the animal be plunged into a solution of extract of belladonna, no mechanical irritation of that portion of the body will cause the tetanic convulsion: the exceptional effect is the same as was produced in Dr. Mayer's experiments by division of the posterior roots; but when some other part of the surface is irritated under these circumstances, so as to procure the characteristic spinal reaction, the resulting convulsions occur in the muscles of the anæsthetic limb, equally with the other muscles of the body. I need hardly point out to you the important practical applications of which this property is susceptible in diseases which consist in an exalted reactivity of the spinal cord.

Of medicines acting on the nervous centres through the blood, by way of stimulation or narcotism, there are a large number; but most of them act so complexly, that the specification of their distinctive actions is at present a matter of immense difficulty. Most of them affect, with more or less completeness, all the nervous centres;—one series of centres, if given in their smaller doses; two or more series, if given in larger quantity; and, under the influence of the same remedy, the phenomena of centric excitement or centric depression may become variously manifest, according to the dose of the agent, and the habit of the individual.

Strychnine has already been adverted to, for its power of exciting the motional centres of the cerebro-spinal system; and this action is one of the simplest with which we are conversant, apparently not

extending beyond those tertiary centres, and such ganglionic centres as are subordinate to them; there is no evidence of mental affection under its use, nor are any subjective sensations excited by it.

Tobacco, perhaps, most nearly represents the opposite action; tending excessively to paralyze the motional energy of the tertiary centres; but its operation certainly extends, in the same depressive manner, to the centre of consciousness—comatose insensibility resulting from its larger doses.

As regards both these agents, it seems probable that the influence exerted by them over the heart's action (the one enfeebling, the other rendering it spasmodic) is effected by descensive sympathy, operating from the cerebro-spinal on the ganglionic system.

I have already shown how the reactive phenomena of the cord are influenced by the peripheral use of *belladonna:* it seems probable that analogous results would be produced, after its ingestion, by its anæsthetic or depressive action on the sensitive centres. It dilates the pupil as much when it is taken internally, as when locally applied; and as in the former manner it operates on the visual as well as the tactual centre of the eye, we find that the perception of light is impaired—an effect which does not arise from its peripheral use. Any interference which its internal use may produce on the reactivity of the cord would apparently arise—not (as from tobacco) by motional paralysis, but by an anæsthetic condition of the sensitive centres, forbidding the transmission of those exterior stimulations which normally excite spinal reaction. In affecting this function, it would act centrally, as I have just shown that it acts peripherally, as an impediment to the receptivity of the nervous system. In Dr. Burton's case* of poisoning by belladonna, there remained, for several days after the patient's consciousness had returned, an almost complete anæsthesia. While the tertiary centres of sensation are depressed by this remedy, the centre of consciousness is remarkably stimulated, giving rise at an early period to delirium, which is characterized by the presence of extreme delusions.

Chloroform and *Ether*, operating by inhalation, seem to work their effects in a similar way; and the explanation which I have just given of the indirect manner in which belladonna becomes the antagonist of strychnine or of tetanus, will explain the palliative influence which chloroform is alleged to exert under similar circumstances. It does not depress the excited reactivity of the motional centres, but disables the sensitive centres from becoming media of stimulation to them.

This class of agents operates little (if at all) on the quaternary centres of the ganglionic system: these subordinate organs sympathize readily enough with the motional variations of their superordinate centres (as we see in the affection of the heart by strychnine or tobacco) but are not considerably involved in artificial anæsthesia; or at least not primarily: if the anæsthetic influence be intense, and the cerebro-spinal motional centres become depressed by it, then

* Medical Gazette, vol. xli. p. 1024.

unquestionably the quaternary centres of the ganglionic system may evince a similar affection.

Opium illustrates in an extreme degree the complexities of operation which obscure the pathology of narcotic medicines. Its most usual method of action in the human subject is to operate chiefly on the centre of consciousness; affecting it mainly in its receptive functions, so as to induce, first, subjective mental phenomena (dreams and imaginations) followed (or, after large doses, anticipated) by an overwhelming comatose insensibility. It rarely produces in the cerebral centres those changes which lead to active or volitional delirium; differing in this respect from alcohol and nitrous oxide. Its operation on the subordinate nervous centres is distinct and different: it excites (sometimes to an extraordinary degree) the motional centres, so that reflex-movements tend to exaggeration: witness that contraction of the pupil to a mere pin-hole which occurs under its influence: witness also the tetanic symptoms (having their origin in the cord) which it produces invariably in some of the lower animals (most of all in frogs) and occasionally in man. It is exceptional in the human subject for the spinal phenomena to be prominent after the ingestion of opium: perhaps our more highly developed encephalic centres are capable of communicating their depressed condition to the subordinate centres, in a manner which less perfect organs would fail to exhibit, and which tends to neutralize for these lower centres whatever primary influence the opium would else exert on them. Opium is not an anæsthetic, except by the production of stupor. Probably the spinal centres of sensibility are among the last elements affected by it. There is one remarkable phenomenon, however, which occasionally arises from the use of opium (or morphia more particularly) and which is referable to these centres. I mean the subjective sensation of itching at the skin—a sensation which is sometimes universal and intense. A few months back, I was treating a gentleman for delirium tremens: his disease resisted the morphia—even in very large doses, and eventually yielded to chloroform; but, after each dose of the morphia, he suffered intensely from this formication, and his disordered fancy (stimulated by the subjective sensation) led him, whenever the morphia was acting, to believe and maintain that his body was covered with swarms of lice. Probably double or triple the dose here given would in this particular instance have produced anæsthesia, as though belladonna had been employed: but I have never witnessed this action.

A most important question as regards the action of opium, and one hitherto very imperfectly solved, is that of its influence over the nutritive changes in parts;—whether that influence be exerted through the motional ganglia of the arteries (so as merely to regulate the local supplies of blood) or consist in a direct chemical control over the activity of molecular change. Of the reality of such influence—in whatever way produced, we have empirical knowledge. In surgical practice, we constantly find advantage in the use of opium, which seems referable to this head, and which leads to its employment as a prophylactic against excessive inflammatory action

in many cases of severe local injury by accident or surgical operation—after extensive lesion of serous cavities especially, where we wish to moderate the determination of blood which is likely to ensue. Many surgeons make large use of opium in this manner, employing it more or less after all capital operations; even where they are not called upon to fulfil the collateral purpose of mitigating pain.

I have said nothing of the action of narcotic medicines on the *secondary centres* of the nervous system; and I know very little about it. M. Flourens thinks himself able to trace some signs of cerebellar affection in the symptoms of intoxication by opium, and still more in those produced by alcohol; and various experiments which he made, by the direct application of these and other drugs to the nervous centres, furnish some confirmation of his view.

My limits will not permit me to dilate on these subjects; but the few examples I have given you may serve, at least partially, to show the sort of inquiry which is needed, and to illustrate that carefulness of selection with which narcotic medicines require to be employed.

LECTURE XI.

Evacuative medicines in relation to Humoral Pathology. Critical discharges in disease; gout, rheumatism, cutaneous eruptions. Humoral disease in condition of latency, and in act of explosion. Medicinal influence over excretions. Excretive drugs having local affinities of action; diuretics; query as to effect on real act of excretion. Vicarious excretion; compensative excretion; diaphoretics in diabetes. Summary of results: Derivative medicines; medicines modifying catalysis of blood. Action of saline purgatives by way of exosmosis; pathology of ordinary constipation; natural or acquired inertness of certain drugs. Supplementary medicines.

Gentlemen: Within the compass of Pathology, I know of nothing so obscure and unsatisfactory as that division of the science which relates to morbid and medicinal changes in the excretory functions.

It is not difficult to say what knowledge ought to be acquired in these respects. We ought to have exact information of the changes which any drug or any disease is capable of producing in the several excretions; and we ought to possess the explanation of these changes, including (first) a knowledge of whatever chemical alterations of the blood precede, accompany, or follow them; and (secondly) a knowledge of whatever mutual relations subsist between different excretions, and how far any given variation in one particular excretion entails of necessity some corresponding variation in another. In other words—the healthy qualities of each excretion being stated by the physiologist, it devolves on the pathological chemist to fix their morbid and medicinal variations, not only simply and absolutely, but likewise relatively to one another, and to the blood. This kind of knowledge—relating to that portion of our subject which abuts on pharmacology, ought to receive its chief elucidations from the professors of the latter science. Hitherto, however, singularly little light has come to us from that quarter.

We are led to an intimate pharmaceutical acquaintance with the *Materia Medica*. We learn the smell of rhubarb, the tests of arsenic, the chemical incompatibilities of iron, the adulterations of quinine or sarsaparilla, and so forth. We become skilful dispensers. We know that bark very often cures ague; that copaiba frequently stays a clap; that cod-liver oil and iodide of potassium between them relieve a good many cases of scrofula; that taraxacum is sometimes useful below the diaphragm, and squill above it. And with this farrago of traditions, the misnamed *science* of *Materia Medica* has remained so contented and so stationary, that at the present moment —in the middle of the nineteenth century—we do not possess a complete medical knowledge of any single article of the Pharmacopœia.

It would be easy for one quite ignorant of medicine to predict,

on general grounds, what must be the result of this state of things; what blind reliance on specifics where they are supposed to prevail; what credulous—perhaps rather what desperate combinations of drugs where we have no traditional specific to trust to. An indifferent shot in a turnip-field does not mark his one bird, and bring it down; he bangs at the whole covey, and thinks it a hard case if he hits nothing. On some such principle as this—scarcely sanctioned in the sportsman, much less admissible in the medical philosopher—we too often discharge our barrels. If the immemorial *certificates* of a specific serve us instead of real knowledge, and enable us confidently to give quinine to one patient, and sulphur-ointment to another—good: but in the absence of such traditions, how many prescriptions are written, which combine at least a dozen different materials, where the prescriber is utterly unable to define the precise errand on which any one of these ingredients is sent into his patient's body. This prescription failing, another of the same sort is written, and another after that; and presently the patient dies or recovers, as the case may be. And in either event, from the absence of a definite principle in the treatment, and from the want of having attached a separate meaning and intention to each drug employed, the pharmaceutical experiment has been too complex for the practitioner to draw any rational or useful inference as to the immediate causes of his success or failure.

Contrast this with what occurs in chemistry or in physics. You wish to precipitate a certain material from its solution: you do not throw in at random the contents of several vials, with a vague hope that one of these reagents may answer your purpose; you proceed with a very definite object, and by appropriate means. If A be present (you say) B will throw it down, by forming such or such insoluble combination—provided (you may perhaps have to add) that C be not present likewise, for in that case C must, first of all, be neutralized: provided also (you may further have to concede) that B be added in a sufficient, and not in an excessive quantity, lest it redissolve its own precipitate. These, or similar allowances being made, the sources of fallacy are just as definite and palpable as the anticipated positive result; and, if your operation should miscarry, you would be able to account for its failure, and to repeat it in a form which—not casually, but certainly—would accomplish your purpose. So, again, if you plunge the wires of your galvanic battery into water, and fail to produce the expected result, you do not fly off to some new arrangement—you do not try wooden conductors, or add twelve additional wires, or attempt to decompose the fluid with your finger and thumb; you know exactly what the hitch must be, that your circuit must be incomplete, or that you have forgotten the acid, or something of this kind; you correct your omission, and you are certain of the result—*certain*, because you know definitely the means to attain it, and are cognizant of their method and principle of operation. On the other hand, when we have given colchicum to six patients suffering with gout, when it has relieved two of them, and has left four unrelieved, we are quite unable to

explain why it failed here, and succeeded there: and consequently, in that unsuccessful majority, we are quite unable to supply the absent condition (whatever it may have been) which was accidentally present in the successful instances, and conduced essentially to their cure.

It is quite indispensable for the progress of medicine—I might say, indispensable for its existence as a science—that our *Materia-medica* should be made subject to a true pharmacology; that its province should cease to be a mere emporium of recipes; that we should have a knowledge of its various elements in their true relation to the living body; that we should give drugs only with a clear perception of their causativeness, and with a definite object before us; understanding the medicine as well as the malady, and taking one good aim at the substance of the disease, instead of discharging a volley at its shadow.

I wish to lecture to-day on some points in the pathology of excretion, mainly relative to the influence of evacuative drugs; and the reflections which I have just made, arise spontaneously as I approach this subject, for the amount of exact information which I can collect for you is, from the reasons I have mentioned, scanty and insufficient. The subject, however, is in itself so very important, that I am unwilling to lose the opportunity of bringing it before you; and I am sure that, apart from any new light you may gather here as to the action of remedies, it will do you good to probe the extent, the depth, the reality, of such knowledge as you may think you possess on these matters.

I. First of all—with respect to the modifications which Disease imposes on the several excretions. That many ailments are attended with extreme alteration in some one or other excretory act of the body, is so obvious a fact that it was recognized in the earliest dawn of medical observation; and the first physicians were almost intuitively led to regard many of the evacuations, thus arising in the progress of disease, as *critical*, and tending to terminate the morbid process. Changes akin to fermentation were referred to the blood, and were supposed to constitute the essence of a disease, which sought its cure in that critical evacuation of certain "peccant humours." These views, which form the staple of the so-called *humoral pathology*, have at various times been obscured and defaced by the admixture of all sorts of error and crude hypothesis: they have been alternately adopted and rejected, without reason and without discrimination. It is only within the last few years that their extensive truth has admitted of exhibition, has been extricated from an atmosphere of fancy or falsehood, and been rationally and experimentally set forth.

Perhaps, at first, I could illustrate to you the line of argument on which humoral pathology depends, better by the instance of a drug than of a disease; but the evidence is alike in both instances. Whenever the exhibition of a medicine, by various and different channels of introduction, produces effects distant and general in the body, there is fair ground for presuming that it operates through

the medium of the blood. When you find (whether you are dealing with some drug of the pharmacopœia, or with a disease like gout or rheumatism)—when you find a first stage of general discomfort and vascular excitement or depression, *followed and relieved* by a second stage, in which particular excretions are increased, or in which some new product is cast off (with or without local inconvenience) there is room to suppose that, during the first stage of these consecutive processes, something has been accumulating in the blood; which something, during the second stage, succeeds in finding an outlet from the system, and so works a cure for the previous inconvenience. You have a familiar instance of this with the iodide of potassium, frequently being able to see how it distresses the patient in various ways, which testify its presence in the blood, till its diuretic action is fully established, and then all these troubles cease. Your chain of evidence is rendered complete by your ascertaining the presence of iodide of potassium in the urine at this point of the case: there it is, representing the *peccant humour* of our medical forefathers, discharged in a *critical* evacuation of urine, and terminating that *fermentation of the blood*, with which the patient was previously feverish and troubled.

You will have no difficulty in applying this analogy to the case of gout. A man has for months a variety of obscure symptoms; general discomfort, bodily and mental; depression of spirits; occasional flitting pains; frequent cramp in the extremities; and perhaps some chronic desquamative disease of the skin. These complaints are individually capricious, coming and going uncertainly; but with some of them the patient continues to labour, and progressively to be more inconvenienced, when at length (having perhaps committed some indiscretion of diet before going to bed) he wakes one night with a distinct feverish attack, and an uneasiness in his great toe. By degrees, the local uneasiness amounts to absolute agony, and becomes attended by the ordinary evidences of acute inflammation—heat, redness, and swelling. Simultaneously with the development of these local symptoms, the patient's febrile excitement subsides. After a certain period of suffering, the toe gets easier, the man convalesces, and he now finds himself, in general health, better and more comfortable than he has been for months. His hypochondriasis is gone; he sleeps well; he has no pains, no cramps, no gastrodynia; and his old skin-disease has almost or quite vanished. Now what is it that has worked all this improvement? He has got rid of his *peccant humour:* at the commencement of the acute attack, his blood was loaded with lithic acid; at the close of the attack, his blood was relieved from that material, which had accumulated in the inflammatory effusions about his painful toe. Cut into the textures there, and you find them abundantly infiltrated with a chalky product, which is the real *materies morbi*—lithic acid in combination with an alkali. Rationally, one might have been pretty sure that this material had accumulated in the blood as the immediate condition of the attack; but it is only recently that chemists have succeeded in demonstrating its presence during the paroxysm of

gout. In the form which I have represented, it might hardly be correct to speak of the disease terminating in a critical excretion; because the morbid product, though excluded from the blood, is not shed and discharged by any normal excreting surface of the body. But if you examine the urine under the same circumstances, you find it overloaded with the material of the disease, which the kidneys are endeavouring to eliminate: and you are very apt to witness, concurrently or alternately with common gout, the occurrence of inflammation in mucous and serous membranes; where, either probably or demonstrably, the same material can be traced as a specific irritant for which the membrane strives to effect a critical evacuation. Look now at a case of rheumatic fever, and you will see that though the chemical demonstration is absent, the general evidence of a humoral origin is complete. Intense febrile disturbance, an evident physical change in the blood, various local inflammations, and profuse acts of excretion, constitute the chief features of this disease, which further tends to run a course of certain duration and to terminate in recovery. The skin and the kidneys are the chief organs of critical excretion in this complaint; and the serous and synovial membranes are the parts in which the insufficiency of that critical excretion chiefly tends to show itself by acute inflammatory attacks. The material which causes these disturbances is hitherto un-demonstrated: we only know that the skin pours out a profusion of acid, and that the urine (which may be either acid or alkaline) is overloaded with effete organic products—urea or extractive matters, or both. This scanty knowledge, so far as it goes, need only testify to some intra-vascular decomposition, dividing its products between those two excretory surfaces: and, in the absence of accurate information, we are unable to decide whether the material thus undergoing change within the blood be a natural ingredient there; whether (as seems not improbable) it be one which, during health, legitimately divides the products of its decay between those surfaces which in disease are rendered the emunctories of its excessive or accumulated presence.

Again, in the phenomena of infected fevers and other allied disorders, we have the strongest evidence of a humoral origin and progress, tending to cure by critical evacuations; but I reserve my remarks on their pathology till I come to analyze the effects of the morbid poisons.

In cutaneous disorders, both acute and chronic, we have abundant evidence of that sympathy between the skin and other excretory organs, which can only be maintained through the circulation; and which suggests here (as previously with acute rheumatism) that errors of growth or function, affecting the skin and other excretory organs conjointly, may have its readiest explanation in some single morbid condition of the blood. Where the disorder is chronic, we have not indeed the additional testimony of constitutional disturbance; but in acute cases of skin disease (even without counting the true exanthemata) we constantly see the eruption preceded by an amount of febrile disturbance which attests derangement or con-

tamination of the blood. Such, for instance, is the slight fever which precedes many cases of erythema, of herpes, of psoriasis, or that intense illness which attends the outbreak of carbuncle: and in these cases it is almost invariable to find the urine more or less sensibly altered in its composition. The determination of blood to the cutaneous surface must in these instances, on the ground of analogy, be considered eliminative in its purpose; but there is an insufficiency of exact chemical evidence on the subject. In some instances of chronic leprous eruption, lithic acid is said to have been found in the desquamated cuticle; but it has never happened to me, in such cases of psoriasis or lepra as I have watched, either to find lithic acid in the cutaneous excretions, or to recognize in them any other material foreign to their ordinary composition: I have not seen more than the evidence of increased discharge of materials proper to the surface. The urine, too, under the same circumstances, is less apt to show new products than to present its characteristic effete materials in modified quantity. Heller describes the urine in herpes as marked by a considerable increase of its chlorides, especially of its chloride of sodium; and he gives a case of pompholix in which the same ingredient was remarkably diminished, while the urea stood at an unusually high figure.

Increased excretion from the mucous membrane of the intestinal canal often gives undoubted evidence of a humoral origin and a curative tendency. I can give you no better illustration of this than the purging which often arises after exposure to the miasms of decomposing animal matter—as, for instance, that which we incur during our prosecution of anatomy. In such cases the sufferer can commonly identify the material which is producing his diarrhœa, as that which had previously been inhaled by him; for it retains its peculiar smell, and imparts it to the increased excretion. Thus, for example, if one spend some hours leaning over the dissection of a dog or a porpoise, or any other animal having a peculiar odour, and if increased excretion from the intestines be the result of this industry, the evacuation presents, quite unmistakably, the smell of the one beast's skin, or the other's blubber. The diarrhœa which often arises after sudden suppression of sweat, and that inflammation of the duodenum which attends large destructions of skin by burn or scald, may partake of the characters of humoral sympathy or metastasis; and in such the blood could be the only medium of communication. The obstinate vomiting which frequently coincides with the invasion of carbuncle; that, which sometimes (together with diarrhœa) attends the latter stages of Bright's disease, when the renal excretion is suppressed; and, in a minor degree, that gastro-intestinal disturbance which accompanies the eruptions of herpes and urticaria; these are other illustrations, in which there may be traced a reasonable probability, and in some perhaps an absolute demonstration, of the gastro-intestinal mucous membrane assuming increased activity as an emunctory of morbific matter from the blood.

In glancing back at the several instances of critical evacuation

which I have adduced, you will be struck with one radical defect in their completeness for demonstration. With few exceptions, we are only able to recognize the change of excretion, generally and grossly, as changes of quantity, colour, and consistence. We have not those accurate chemical analyses which scientific pathology would require; and we are consequently unable to state the relation which subsists between the essential disease and these several excretory efforts. Our knowledge of them is inexact, and chiefly inferential.

A peculiarity in some of the diseases to which I have referred —in gout, for instance, or rheumatism, or carbuncle—consists in what I can call by no other name than the *explosiveness* of their onset. A man goes to bed apparently in his ordinary health; presently he wakes in the first stage of a disease, which at once establishes the acutest known forms of local inflammation, or which assigns to his skin, his kidneys, his shut sacs, such an amount of materials for excretion, as occupies all these organs laboriously and continuously during some weeks. Are we to suppose that the various excretions discharged at so many different vents, during the protracted course of a rheumatic fever, have collectively accumulated in the blood previously to the commencement of the attack? I think the evidence will hardly justify us in adopting this conclusion: the facts rather point to the probability that some sudden decomponent change commences at a particular moment in respect of some accumulated ingredient of the blood (normal or abnormal) and that the separate results of this explosive decomposition, corresponding more or less exactly to the normal products of blood-waste, pass to the various excretory surfaces with which they have nearest affinity. In respect of the diseases here more especially alluded to, it seems in a high degree probable, that the period *anterior to the attack* has, for its pathological characteristic, the accumulation in the blood of a material not identical with the peculiar excretions of each disease, but naturally capable of conversion into such excretions; that (for instance) the interval between two paroxysms of gout would not be attended by the retention of lithic acid in the blood, but, by the excess there of whatever ingredient naturally furnishes that acid; that this ingredient (whether normal or altered) by some cause or other, is hindered from undergoing its regressive chemical changes as fast as it is formed; that it consequently accumulates in its original character, instead of being decomposed for excretion; till presently some new momentum is given, or some difficulty overcome, and the accumulated material runs its natural progress of change in an explosive and tumultuous manner. If this be a true interpretation of the phenomena, —and I hardly see that any other is possible—these diatheses would be capable of producing two classes of ailment; one by reason of the retained material itself, another by reason of its products of decomposition. I have already cursorily alluded to the possibility that some such relation as this, between primary and secondary blood-products, may account for the association of certain morbid

symptoms with the *latency* of recognized humoral diseases; as, for instance, of chorea and rheumatic fever; the primary accumulating product forming the irritant of one organ; the secondary excretive product forming the more explosive irritants of other organs. I have likewise suggested, as a converse case to this, that some similar inter-dependence may possibly account for the association of tubercle and fatty degenerations; the former depending on a primary blood-disease which is capable of showing its secondary products in the latter. (*See* Lecture IX.)

II. Such observations as those I have illustrated to you, many of them dating (as I mentioned) from the earliest records of medical experience, and appearing to bear constant testimony to the critical and curative tendency of augmented excretions in a great variety of disorders, have naturally had great influence in medicine. Evacuative drugs have held the most important rank in the *Materia-medica:* and there have been times, even in the modern history of practice, when the balance of medical opinion has inclined itself towards the imagination, that by appropriate evacuants any conceivable disease might be expelled from the body, in the form of urine, sweat, stool, or vomit. All scientific generalizations, especially such as fall within scope of the popular eye, become liable to these preposterous excesses of application; but it would be a fatal mistake for the interests of medicine, if, on account of such extravagances, we refused to recognize those invaluable indications which may be derived from a careful study and a rational application of the humoral pathology.

Taking for granted, then, that we ought to follow the suggestions of Nature as to the curative tendency of certain excretions, and that we ought, in a large variety of cases, to adapt our treatment to this evacuative purpose, you will perhaps think that the object is an easy one. You will remember the emmenagogues, the diuretics, the sudorifics, the cathartics, the sialagogues, the errhines, the expectorants, of the dispensary; and you will feel assured that, with these resources, you must be omnipotent against humoral diseases—that, with a pharmacopœia so plentiful and so nicely arranged, your only difficulty can be that of selection—the merest *embarras de richesses.*

It will surprise you perhaps to be told, unless you have ascertained it in practice before coming to learn it from pathology, how very much delusion lies under cover of those fine names, and how singularly little real or useful power we possess over the organs of excretion.

If we inquire into the physiology of these organs, we find, with them as with all others, that their natural stimulus is the blood; and we are able to say of them generally, that, *cæteris paribus*, their activity of function varies proportionately to the abundance of blood traversing their capillary vessels. To increase the circulation of blood through an excretory organ would appear, then, an easy

method of augmenting its characteristic excretions. In the abstract this may be true, but practically it has a very important qualification. The blood is capable of exciting in the several organs of excretion their appropriate acts, only because, by means of its own decomposition, it furnishes to the growing elements of each several organ that specific material which it is their function to appropriate and excrete. If, for instance, the blood were divested of the ingredients of urine, its circulation through the kidney would be fruitless. It is the law of those nucleated cells which form the bulk of all excreting organs, to grow and expand by the appropriation of certain specific materials, and of these only: a cell in the liver fills itself with one stuff; a cell in the kidney with another; and so long as the blood can give them this special pabulum, they grow more quickly and more abundantly, in proportion as their circulation is increased. But, on the other hand, the increased afflux of blood to an excreting organ can serve to stimulate that organ's excretory acts only so long as the blood is ready to yield to the organ its characteristic materials for excretion. Hence it would appear probable that an excretion can be permanently augmented only by an increased formation of its characteristic materials in the blood; and that the artificial production of hyperæmia in an organ, apart from the condition just specified, could only give a moment's expedition to the process of discharge.

In this argument I assume, as an unquestioned fact, that eliminative organs *do not form* the materials which they excrete; that they merely appropriate from the blood certain elements which existed there previously to any act of excretion. The best illustration of this truth is given in the fact that, after absolute removal of both kidneys in the lower animals, urea rapidly accumulates in the blood, so as to become detectible by analysis, and soon in quantities sufficient to destroy life by narcotism: and we are constantly able to observe the same effect in the human subject, where the kidneys are so disorganized as to be incapable of purifying the blood.

It would appear, then, that while the blood, either mediately or immediately, undergoes those important chemical changes which result in its decomposition and decay, the products of this process have their pre-ordained outlets from the body, and, so fast as they arise, become evolved; each, as it were, at its own pole of the galvanic battery. I know nothing better to compare it with than the phenomena of galvanic decomposition; you see the blood distributed with uniform qualities throughout the whole area of the circulation, and you see the products of its decomposition appearing with their characteristic signs at the liver, the kidney, the skin; just as, when you plunge the wires of your battery into a trough of water, you get oxygen evolved at one pole, and hydrogen at the other, while the intermediate material remains apparently unchanged. And to apply that analogy somewhat further (though, by the way, I must beg you to understand that it is merely chosen for illustration's sake, and that I have no intention of suggesting to you that the vital pro-

cess in question is of an electrical nature), I would point out this for your notice: as you are quite sure, in decomposing water, that for every volume of hydrogen at one pole, there must be a corresponding half-volume of oxygen at the other, as you are quite sure that, if the gas be not evolved, it must have spent itself in oxydizing the metal of that opposite wire, so with the manifestations of secretion. You cannot deal with them singly: if the essential ingredients of urine, bile, or sweat, be formed in excess, you are quite sure that certain other ingredients *complementary* to them must have been formed in excess likewise. Supposing, for a moment, that the liver and the kidney were the only organs to be considered, it would be a chemical impossibility for the blood to furnish material for one of these glands without likewise evolving, as a necessary residue of that process, the characteristic elements of the other secretion. As an obvious illustration of this, I may cite an interesting observation by Dr. Bence Jones, in respect of the digestive process: when much acid was secreted by the stomach, the urine was found to be alkaline: the excess of acid in the stomach was hydrochloric, and the free alkali in the urine was fixed alkali, and not ammonia: in extreme cases the alkalinity lasted for four hours; as the free acid was absorbed from the stomach, the urine became acid; and this reaction increased, until it affected litmus-paper intensely.

It would appear, then, that the only natural means, for giving increased development to any particular excretory function of the body, would consist in providing for the increased formation of certain specific materials within the blood; and that this increased formation cannot possibly arise as a single local process, but must involve an affection of the entire chemical economy. And it would appear further, that an augmented determination of blood to the excreting organ can only serve to facilitate the process, in proportion as that fluid has previously been charged with the materials to be eliminated.

Now, Gentlemen, all the power that we possess of increasing, or appearing to increase, individual excretions, by means of medicine acting through the blood, admits of explanation on the principles which I have stated. We add to the blood the ingredient of some one secretion, or more; and in the increased secretions we find the pharmaceutical material which we have given. Here, however, I ought to state to you that the appropriating power of the various excretive organs is not limited to the exact materials of their normal stimulants. A certain latitude of operation is allowed, and very few chemical agents (if any) can enter the blood without finding, as it were, some road prepared for their escape from the system—some organ or other ready for their excretion. Thus, for instance, iodide of potassium is quite foreign to the animal economy; it has no counterpart in any natural excretion; but so soon as a sufficient quantity has been taken to impregnate the blood, it immediately begins to excite the kidney and to be largely eliminated by it. Accordingly, iodide of potassium (as well as various other salts),

though perhaps inferior in diuretic force to the natural constituents of the urine, may certainly be considered as acting in the same manner and under the same law.

But how far may this fairly be called increasing the excretion of urine? Suppose, for instance, that half a drachm of nitrate of potass be taken daily by a person in good health; suppose this continued for a fortnight; what will be the total result? More blood will have traversed the kidney; more water will have been secreted; and that waste of water will have been repaired by an increased thirst, calling for drink in proportion; and the increased flow of water will have carried off with it the nitrate of potass, and for the first twenty-four hours will have appeared to increase the urea and the lithates; that is to say, it will have given facilities for their elimination; it will have washed out the tubules of the kidney, and have cleared away all that there was to be cleared; but, except in that almost mechanical process, it will have done nothing for the characteristic excretions of the gland. The urine of the fortnight would be, so far as we know, only the ordinary urine in all respects but one; in addition to its ordinary constituents, it would contain seven drachms of nitrate of potass and a certain additional quantity of water—if, at least, water had been taken in proportion to the thirst. Most of our milder diuretics let their action be resolved into this: that the excretion excited by them consists of the drug itself, *plus* water.

Under the influence of more violent diuretics (such as cantharides or cubebs) pressed in large doses, so as to cause great irritation of the gland, something different occurs: the excretion is evidently hurried: it contains albumen and tubular epithelium—often blood; it presents at first an increase of lithic acid, apparently at the expense of the urea, and subsequently a decrease of both these ingredients. Finally, so soon as the kidney is relieved from the continuance of these irritating drugs, the specific gravity of the urine (which has already begun to decline in spite of the largest doses) suddenly falls to 1007 or 1008, is quite destitute of lithic acid, and contains exceedingly little urea. These facts (given by Heller as the result of observations carefully made by himself at Vienna) show that the extreme action of the so-called diuretics consists in bringing away the products of urinary excretion in an immature state, mixed with the evidences of inflammation; but they render it little probable, that any purificative action can thus be exerted on the blood: and Krahmer, after performing on himself a hundred and three experiments, of which forty-one were with the so-called diuretics, found that on the whole he passed more urea, more lithic acid, and more of the other solid constituents of urine, without the exhibition of those drugs than with their assistance.

But are there no means, you will ask, of increasing the flow of *real* urine. Can we do no more than add water? Can we invent no real and genuine diuretic, which shall make the urine stronger in its specific ingredients, as well as more plentiful in its flow? Undoubtedly we can, though perhaps in a very different sense to that

supposed in asking the question: *e. g.*, Lehmann, a German analytical chemist, found that by exercise he could increase the proportion of urea in his urine from about 30 in the 1000 to upwards of 45.

I say this is not quite the sort of result wanted, because I presume the giver of diuretics expects that his drug shall be *specially* and exclusively diuretic; whereas, in the case just quoted, the effects of exercise, no doubt, were to be traced in very many other secretions: in sweat, bile, and so forth. It was, in fact, an illustration of what I have already stated to you, that such secretions are secondary results of a previous chemical change in the blood; the strong exercise and attendant waste of muscle, the increased oxidation of blood, the profuse perspiration, all these were elements in the production of that increased renal secretion. The kidney secretes all urea that is brought to it, and on this occasion, more than usual was brought, because of other chemical changes passing simultaneously in the system. But I can give you another case from the same chemist. He took a scruple of *Thein* (the alkaloid principle of tea) at bedtime; the next morning he found his urine contained about twenty per cent. more than its normal quantity of urea. This would, at first sight, appear a case of true diuresis; and, as nothing is said of other secretions, I will assume that they were not increased; but if you will call to mind the chemical constitution of the principle referred to, you will see that in the course of oxidation, it might easily reduce itself to the very formula of urea; and I cannot but suspect that something of this sort must have occurred with it, while within the blood; and that thus, reaching the kidney, not as thein, but as urea, it merely appeared in the urine just as if in the latter form it had been artificially injected into the veins. The same effect is produced, and in the same manner, by the injection of lithate of ammonia into the veins, or by its reception in the stomach; for as it enters the circulation, and becomes oxidized, part of it is transformed into urea, part into oxalic acid; both which materials make their appearance in the urine.

I have chosen the kidney for these illustrations, because we have good opportunities of watching its excretory acts; and likewise, because in practice you will hear a great deal about diuretics, and it is as well that you should know how much, or rather how little, can be done with them. And while I am on this subject, I may show you, as a practical inference, from what I have been stating—a distinction as to the cases in which diuretics can usefully be employed. Suppose that you have a case of ascites dependent on disease of the heart or liver, and you give nitrate of potass, or acetate of potass, or turpentine, as a diuretic, you will have your drug carried off by the kidneys, and with it an increased quantity of water; and if you press your remedy, you will by degrees drain off a considerable quantity of the peritoneal effusion. And in such a case, your diuretic may possibly be a well-chosen remedy. But suppose the case to be one of effusion (more generally anasarca) from disease of the kidneys; such anasarca, for instance, as often accompanies Bright's disease;

and if it were proposed to give a saline diuretic, you would, I hope, repudiate the proposal. If the blood were examined in such a case, you would find it already containing more than its proportion of the natural diuretic salts; competent knowledge of morbid anatomy would tell you that these are detained in the blood only because of the diminished secreting structure of the kidney; and the addition of a diuretic drug to the blood could do nothing but increase its unnatural state, and perhaps aggravate the kidney-disease by the determination of a larger flow of unavailable blood. It is in such cases as this, that diuretics add materially to the sufferings of the patient, causing albuminuria or hemorrhage.

I believe that what I have stated with regard to the kidney applies equally to all excreting organs; that their best stimulants are their own characteristic excretions; that if these exist in the blood, no extraneous stimulation can be so effective as they, for exciting the organ to which they belong; that if they do not exist in the blood, no special stimulant of the organ which ought to evolve them can do more—even in its highest doses, than bring away from that organ the results of an immature excretory process admixed with those of inflammatory excitement.

The next question in the pathology of excretion is this; can one excreting organ act vicariously for another? Can the kidneys act for the skin, or the skin for the bowels? or, in short, what does occur when a particular secretion is arrested? A great many cases of the kind are talked of, but, on circumstantial inquiry, they appear very unsatisfactory. As far as I can ascertain the truth, it appears to be thus: when a secretion is suppressed, if there be in the body another organ naturally evolving similar, or partially similar, materials, that organ will, *so far as the agreement of material extends*, but *no further*, adapt itself to the necessity of increased action. And organs which in this manner naturally secrete very similar materials, may be considered (but, again, only so far as the similarity extends) to antagonize one another's activity. Thus, in respect of water, the skin naturally antagonizes the kidney; if the skin sweat profusely, the urine will be in small quantity; if the urine be excessive (as in diabetes) the skin becomes dry.* Accord-

* There can be little doubt, I apprehend, as to the propriety of counting the dryness of skin in diabetes for a *result* of the aqueous drain which that disease establishes at the kidney; and I therefore use the fact, without any hesitation, as illustrative *e converso* of the physiology of compensative excretion. I may take this opportunity of adverting to the pathological ignorance which is implied in the endeavour to cure diabetes by diaphoretics—an endeavour made (we may presume) on the supposition that, if the *flow* could be diverted from the kidney to the skin, the disease would, *ipso facto*, be cured. In such treatment, it seems forgotten that the flow (as such) is the merest accident of the disease, and perhaps rather advantageous than otherwise. The disease essentially consists in a faulty assimilative process, which gives an immense formation of sugar as a morbid result of the conversion of food. This sugar being in the blood, Nature's best course, under the circumstances, is to get rid of it, *plus* water, by the kidneys. The patient eventually dies—not because he passes much water, but because he discharges, in the form of sugar, that which ought, in the form of some protein compound, to renew the tissues of his body. If diaphoretics were so successful as to carry all the water of his system to the skin rather than the kidney; and if, as an immediate result of this energetic doctoring, he should cease to pass *syrup* by one outlet, and should begin to pass *lump sugar* by another, what difference could this make in the final issue of the case?

ingly, in the treatment of disease, the skin may be made to transpire a great proportion of water which otherwise would be discharged by the kidney: but the skin would be quite incompetent to relieve the kidney by eliminating urea for it, because that material does not naturally enter into the cutaneous secretion. Probably the only instance in which the relief can be complete is where there are double organs (kidneys, breasts, testicles, for instance), and where, after the loss of one, the surviving other acquires an increase of activity that prevents the system from suffering inconvenience.

In other cases, all the material which cannot escape by the natural excretory surface, or by some other in affinity with it, accumulates in the circulation sometimes to a considerable extent; and then, as all secretions are evolved from the transuded liquor sanguinis, all become more or less contaminated with this retained product, though none are sufficient to discharge it from the system.

But, though the instances of true vicariousness in secretion scarcely extend beyond the discharge of water, yet there are some instances —or, at least, there is one good one—of compensative secretion approaching very nearly to the vicarious character. You are probably aware that diarrhœa and vomiting are very common incidents in the progress of Bright's disease, when the function of the kidney is much interfered with; and from the recent experiments of two French physiologists, I suppose this symptom must be considered a case in point. Messieurs Bernard and Barreswil extirpated the kidneys of dogs, and watched the result. It consisted of two stages: there was a first stage, marked by increased gastric and intestinal secretion, especially the former; and this new secretion, instead of being periodic, as the ordinary digestive secretion is—instead of having any definite relation to the meals of the animal, went on continuously, just as the secretion of urine would do. During this stage, which lasted above two days, the animal appeared well, digested his food properly, and had no trace of urea in the blood. The second stage was marked by the cessation of this gastric secretion, and by the appearance and accumulation of urea in the blood, which presently produced its characteristic poisonous effects on the brain, and soon killed the animal.

Now thus far the case looks as if—at least, in the earlier stage of the experiment, the gastro-intestinal mucous membrane had taken on itself the function of the kidney, and had eliminated urea. However, it had not accomplished this vicarious secretion; it had not discharged urea, for the fluid contents of the stomach and intestines were carefully examined, without betraying a trace of that substance; but they contained a very large quantity of ammoniacal salts, naturally foreign to them—so large a quantity, that it was impossible to doubt that the urea had undergone in the blood that transformation into carbonate of ammonia to which it is so prone, and had in this form effected its escape into the intestinal canal. It appeared, however, in all the experiments, that this compensative action could not long go on; the intestinal membrane was apparently unable to keep pace with the necessities of the system, and death soon ensued.

Some pathologists have believed that certain changes in the liver may be considered compensative for previous interference with the lung; as, for instance, where enlargement of the liver or its fatty degeneration occur in connection with phthisis, or with defective oxygenization of the blood in hot climates, and under other circumstances of extreme bodily inaction, as with the celebrated Strasburg geese. There is room for doubt in respect of these cases, and especially as to the first of them, for (as I told you in a former lecture) fatty degeneration of the liver often occurs independently of disease in the lung, and, when in connection with it, is not by any means invariably proportionate to the pulmonary disease. Nor is it, as on this theory it should be, equally a concomitant of other chronic pulmonary diseases; it attaches itself to phthisis by reason apparently of the diathesis in which that complaint arises, not by reason of the interference with respiration, which it eventually produces. Still, I think it may be admitted in general terms, that the elimination of hydro-carbon at the liver will increase when the blood is imperfectly aerated at the lungs, and this may be considered a compensative action, facilitated no doubt (according to a rule I have already given you) by a certain natural similarity in the chemical functions of the two organs.

So far then, Gentlemen, as we have hitherto advanced with the pathology of excretion generally, the following principles would appear established:—

1. One organ can excrete for another only such materials as are common to both. All organs can excrete water, and perhaps certain salts, for one another. Thus far—*i. e.*, in respect of such materials as are common to both—one organ may be said in health to antagonize, or in disease to act vicariously for another, but no further. There may be a sanguineous derivation from one to another, but not a substitution of activity.

2. To a very limited extent, certain retained excretions may undergo in the blood a chemical change, which brings them within the means of appropriation of some other organ than that to which they specially belong; thus, in the experiments I cited, urea for a time seemed to be excreted from the system by the mucous membrane of the stomach—not, indeed, as urea, but as carbonate of ammonia; thus, again, carbon and hydrogen, when incapable of passing off in their respective gaseous combinations, seem liable to be secreted as fat.

3. By means of drugs having special organic affinities—such as cubebs for the kidney, elaterium for the intestines, arsenic for the stomach—we are able almost indefinitely to produce and accelerate, in the excreting surfaces of the body, certain changes, which tend in each case to eliminate the particular drug with more or less aqueous exudation; but which fail to augment, or, at the utmost, only momentarily augment, the discharge of material specific to the surface. And,

4. As these accelerated molecular changes always involve the occurrence of atrificial hyperæmia, so we may expect, and we do

really find, that excretions thus abnormally excited will always contain evidence of the congestion we have induced, presenting (just like inflammatory effusions) the several grades of albuminous admixture, to which presently the fibrin of the blood, and subsequently its coloured particles, are added in increasing proportion. Under the influence (*e. g.*) of cholera or elaterium, there is set up along the mucous surface of the intestines, a condition of molecular excitement, under the operation of which they first shed their mature epithelium; next, a profusion of unripe epithelial growth, giving the reactions of albumen, and floated in a profusion of water; next, a fluid which constantly becomes more like the serum of the blood, contains flakes of coagulated fibrin, and often gives evidence of the rupture of capillary bloodvessels.

And as regards the practical application of these powers, it is obvious that by means of them, as by a blister to the skin, we can effect very decided derivations of blood—can render one surface vascular, more or less, at the expense of another: we can likewise carry away, by any of the excretory surfaces, an indefinite quantity of a fluid possessing more or less according to the degree of stimulation, the chemical characters of serum. But the derivative processes thus induced are so essentially of an inflammatory nature, that we ought very much to hesitate in having recourse to them needlessly or violently; and, above all, in respect of solid and complicated organs of excretion, such as the liver and kidney, where every inflammatory excitement leaves its permanent traces of mischief, we ought not to select them for the working of this vicarious irritation without the fullest conviction of necessity.

From the ground we have already gone over, you will have gathered misgivings, that with some show of power against humoral diseases we really possess extremely little true and available influence. For while, unquestionably, we are enabled to determine blood to this organ, or to that; while we can confidently insure that our senna shall pass out by one channel, our cantharides by another, and in either case carry serum with them; we find this ability of little service in respect of humoral disease, by reason of what I have already explained to you. If rheumatic fever forms with explosive rapidity certain materials *congenial* to the excretion of skin and kidney, the use of diaphoretics and diuretics is obviously superfluous; and in the latter more complex organ any such treatment would of necessity do more harm than good. We see the solid materials of the urine largely increased in rheumatic fever: we have the clearest evidence that the material already in the blood is a most efficient diuretic; so efficient, that not infrequently, like cantharides, it produces hyperæmia enough to cause the excretion of albumen or of blood; and we are acquainted with no medicine (unless water be so considered) which can at all facilitate the process thus energetically commenced by nature. Derivatively we may act no doubt on the mucous membrane of the intestines, and may establish there a counter-irritation in relief of the inflamed organs; but against that which is specific in the malady, our purgatives are utterly

powerless, and apparently contribute no more to vent its distinguishing "peccant humours," than, in a case of suppression of urine, they would suffice to eliminate urea from the system. Whether a material, seeking to pass off by the skin and kidneys, be normal or abnormal; whether it be urea, or that animal matter which loads the excretions of our rheumatic patients, we have no sufficient reason for believing that we can convert that diuretic material into one voidable by the intestines. By any excreting organ we can only evolve those elements which have a specific and elective affinity for its action; and where this affinity prevails, I repeat that the elements themselves work their own discharge with at least sufficient rapidity. Obviously then, Gentlemen, if the science of medicine is to find the means of affecting the course of humoral disorders, we must look further into the operation of drugs than the superficial evidence of their various local affinities. Our only known power of qualifying the specific materials of any excretion lies much deeper in the subject. It lies in such means as we possess for accelerating and retarding the waste of tissues and blood, or that metamorphosis of their material which sooner or later furnishes the elements of discharge. At the head of these means stands bodily exercise, with its attendant increase of oxygenization, as the natural and by far the most efficient stimulus of the organs of excretion. As to the question, whether there are any drugs which control this process, either to increase or diminish it: here exactly it is that our ignorance displays itself, and that we find our inability to cope with the difficult problems of humoral pathology.

It seems probable that *water* promotes these changes in their normal direction: Becquerel found that, by increasing its use, he could likewise increase the true urinary excretion—that of urea.

There are reasons for believing that mercury occasions in the blood that dissolution of certain materials which is preliminary to their excretion; for first of all (just as with a true humoral disease) there is a period of general uneasiness and febrility; this presently gives way to a second stage of its influence, in which a variety of excretory acts occur with unusual activity; while any effused inflammatory products tend to re-enter the blood, and their fibrin undergoes disintegration. It is not easy to say, whether these phenomena are in the normal direction of chemical change, and whether they affect all the retrogressive elements of the blood; but in one respect the excretions thus evolved obviously differ from the more leisurely productions at the same surfaces—they are more fetid, and therefore probably less oxidized. Likewise, as with all excited excretions, they are apt to become inflammatory; in mercurial ptyalism the saliva is abundantly albuminous.

Antimony seems likewise, and in the same manner, to accelerate the destructive metamorphoses of certain elements of the blood; and indeed (since the recent researches of Dr. Mayerhofer) we know more about it than about other drugs of the same class. Without materially altering the proportion of coloured corpuscles in the blood, it produces a marked diminution in its other solid ingredients, and

reduces the fibrin to about a third of its usual quantity. Coincidently with this change occur the various known acts of increased excretion; and in the urine (which has been especially examined) the waste products of the economy are found in excess—especially the urea, of which there is discharged half as much again as is normal.

What other drugs may act in this manner I am unable with certainty to inform you; but when you find any which, like these, tend to affect several excretions simultaneously, you may have reason to suspect that such is their *modus operandi.**

Such drugs, then, as mercury and antimony, when introduced into the circulation, represent exactly the phenomena of true humoral diseases; they effect or hasten a definite metamorphosis in the blood, under the influence of which the materials for excretion become sensibly increased; they do not stimulate the organs on which they act by means of any specific affinity between those organs and themselves (as cubebs stimulate the kidney) but excite their actions indirectly, evolving for their use, from the elements of the blood, a larger proportion of that which it is their normal function to eliminate; and unlike those evacuative drugs which effect their purpose solely by reason of their local affinities) these *catalytic* medicines, if I may venture to call them so, do not merely add themselves to the excretion which they provoke, as nitrate of potassa adds itself to the urine; for no quantity of mercury mixed with saliva would render that fluid fetid.

Of medicines acting antagonistically to these we have little accurate knowledge. Dr. Boecker, of Radevormwald, who has recently begun to investigate the subject in a most philosophic spirit, and with extreme minuteness, has hitherto not made progress enough to throw very much light on its obscurity. With respect to articles of diet he has found, however, that the effete products of the economy diminish under the use of *wine*, *sugar*, and *coffee;* and so far as one can gather a clue from this and from the first steps Dr. Boecker has made in regard of the catalytic medicines, it seems not unlikely that many of the so-called tonics will be found opposed to the destructive changes of the blood, and that their medical efficiency may relate essentially to this opposition. It would be of great interest to ascertain, in this respect, what is the operation of quinine.

It will be obvious to you that our hopes of dealing successfully with humoral disorders depends altogether on the event of such investigations as these—investigations which never can be profitable, unless, like Dr. Boecker's, they include an account of every indi-

* I do not mean that the apparent excitement of several excretions simultaneously is in itself conclusive evidence of a medicine acting catalytically on the blood, for compound drugs may divide their elements between several organs. Acetate of ammonia, for instance, has the reputation of being diaphoretic and diuretic: it might fulfil the one purpose, by means of its ammonia, which would naturally tend to the kidney for elimination; the other, by means of its acetic acid, for which the skin would naturally be an emunctory. Rhubarb appears probably to divide itself in a similar manner between the kidney and the intestinal canal; and many other instances of the same possibility might be adduced.

vidual excretion, and base themselves on a profound study of the natural metamorphoses of the blood.

The only certain power which we hitherto possessed over the development of the blood is that of increasing the growth of its characteristic cells by the internal exhibition of iron; and, as their growth undoubtedly extends an influence over the other ingredients of the fluid, we may account this discovery as one of the very greatest practical value.

But, if we are to acquire a power of arresting the changes or deflecting the products, of explosive humoral diseases, this can only become possible by an exact knowledge of the condition of blood prior to the explosion; it must consist in a knowledge—not only of the materials of disease as they are ultimately excreted from the body, but at least equally of the previous condition in which they subsisted in the blood. When that knowledge is attained, and when pharmacology has become a science, by gaining a true insight into the operation of medicines on the blood, then the indications of practical medicine in respect of humoral disease will become clear and plain; and we shall be able to anticipate and prevent the outbreak, or even directly to arrest the progress, of these disorders with more certainty of success than we now feel even in the humbler endeavour to moderate their violence, and relieve their pain.

In connection with our subject, there are still two or three points to which I may briefly advert.

Some medicines are said to affect the excretions without having previously entered the circulation. Poiseuille has endeavoured to explain the purgative action of certain saline medicines as a simple phenomenon of exosmosis. He parodied a purge with his endosmometer: he found that serum would pass out of it, through animal membrane, into solutions of sulphate of soda, into Seidlitz water, into sea water. The profuse discharge which follows an ounce-dose of sulphate of magnesia consists of nothing more than the ordinary excrements with the addition of the purgative salt and of serum from the bloodvessels.* Therefore, at first view, there is nothing in the facts inconsistent with Poiseuille's theory; and an Italian physiologist, Dr. Bacchetti, has given further development to the doctrine, by showing that the exosmosis of serum into the saline solution is very much increased when an artificial current is kept up, which (just

* Limits of time and space hinder me from following to any extent the subject of cathartic evacuation, and we are not possessed of any very perfect knowledge of its pathology. I may observe, however, in passing, that a very important element in their operation consists in their hurrying away from the intestinal canal a mass of material which otherwise would be absorbed. Among this material must be counted some elements of the hepatic secretion, since there seems good reason to believe that all the ingredients of bile do not normally leave the body with the feces, but that some of them undergo reabsorption into the blood. On the importance of this operation I am unable to form an opinion, but I wish it to be observed as fact, that in the action of purgative medicines there are two elements to be considered: first, their elective affinity for the gastro-intestinal mucous membrane as their channel of excretion, and their consequent derivative power in that direction; secondly, their accidental influence in diminishing the absorption, from the intestinal cavity, of matters essential or subsidiary to nourishment.

like the circulation of blood in the living body) constantly brings new portions of the albuminous fluid within the sphere of attraction of the saline one. It is argued further, that some single salt will act as a purgative or as a diuretic, according to its dilution; will purge (by exosmosis of serum) if it be given with little water; will be absorbed and act on the kidneys, if the proportion of water be largely increased. There is much plausibility in all this, but I doubt if it will bear accurate inquiry. No dilution of sulphate of magnesia prevents it from being a purgative when given in sufficient quantity. No concentration of syrup, or of mucilage, will convert these agents into purgatives, as (on the above theory) it apparently should. I have given half an ounce of nitrate of potass twice and three times a day, in a tumbler of water, without producing that purgative effect, which, in respect of its density, and by comparison with sulphate of magnesia, should be expected from its exosmotic influence. The cathartic mineral waters are of very much lower specific gravity than the serum of the blood; of lower specific gravity even than the serum would be in respect of its saline contents alone. Half an ounce of sulphate of magnesia, taken in solution, and acting as a purge, brings away with it far more than enough water to reduce it below the specific gravity of the serum. It seems almost certain, by reason of these objections, that the exosmotic theory of the action of purgatives is an insufficient one. Probably they all enter the circulation; and the difference of action is resolved into this; that the kidney suffices, without the aid of another organ, to discharge any small quantity of them which may be in the blood; but if their presence be more copious, the intestinal canal co-operates for their discharge. To this it must be added, that many saline medicines, like other drugs, have definite local affinities, and maintain their adhesion to one eliminative organ, without any regard to differences of dose or dilution; nitrate of potass and iodide of potassium (short of poisonous doses) are not convertible into purgatives; nor am I aware that any dilution of sulphate of magnesia will render it a diuretic.

It would obviously be foreign to my subject to consider at any length the use of purgatives, as antidotes to the ordinary forms of habitual constipation. I will merely point out to you what seems to me the guiding principle in the matter. In an infinite majority of cases, the disorder has nothing to do with defective excretory function, either in the mucous membrane (on which ordinary purgatives work the results of their elective affinity) or in the appended glandular organs. It arises in *indolence of reflex-action* in the muscular coat of the intestine; sometimes essentially morbid, as depending on low nervous energy in the special ganglionic centres of the canal; sometimes artificial, as the result of habits, which have been originally induced by faulty exertions of will in resistance to the periodical suggestion to stool, and which have accustomed the ganglionic centres to react only on more than their normal amount of stimulation. In all these cases, the act of defecation, *relatively to the blood*, is sufficiently executed by its normal organ—the mucous

membrane; but it remains incomplete *relatively to the body*, by reason of defective irritability in the muscular fibres, which omit to extrude from the intestinal canal the collected residue of digestion, with whatever materials of excretion have accrued from the mucous membrane and from the glands. Such collections become dry and lumpy, in consequence only of their prolonged retention. Evidently, then, the *immediate* cause of the inconvenience is the non-fulfilment of a certain mechanical function; and, just as evidently, the best *palliatives* must be such as will most nearly imitate, or most naturally provoke, that absent mechanical process. It would be an error habitually to effect by colocynth what a clyster could equally accomplish, just as it would be foolish (if possible) to substitute diaphoretics for soap and water; but still more erroneous it would be to employ either colocynth or clyster, when a slight correction of diet may answer the purpose naturally. The normal method of defecation is by way of tactual stimulation of the mucous membrane: this stimulation is effected by the undigested particles of food; their extrusion by the muscular fibres of the intestine is the reflex result. The rationale of the use of brown bread and fibrous vegetables by costive persons is, that the larger proportion of indigestible stuff in these substances renders them more active stimulants to the peripheral nervous expansion of the intestine. The *permanent* cure of defective reflex action in the intestinal canal, is a matter relative to the general pathology of innervation; it cannot possibly be attained unless the treatment of each individual case be undertaken conformably with those principles which I have endeavoured to indicate; not by a constant make-shift repetition of inappropriate purgative drugs; but by supplying, as naturally and as simply as possible, that very condition which is wanting to the process of defecation, while, simultaneously, measures are taken to repair (by appropriate tonics) the defective innervative energy of the ganglionic centres, or to disaccustom the canal from the habit of indolence which it has been permitted to acquire.

There are some medicines which traverse the intestinal canal, without undergoing change; or, which undergo only such change, as precludes the possibility of their absorption. Oxide of zinc illustrates the first occurrence. Heller has witnessed its exhibition up to two doses of two drachms daily, without finding a trace of it in any other excretion than that of feces: and there he has succeeded in finding the entire quantity taken, still in the very same form as that in which it had been exhibited. Obviously it must have been quite inert.*

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* I entertain no doubt, whatever, of the accuracy of Heller's observations, and am, therefore, convinced of the inertness of the drug. It is amusing, with this conviction, to read the following *tradition* of its uses, which I transcribe from one of our most judicious and practical writers. "Internally, it has been used chiefly as a tonic in epilepsy, and sometimes with advantage. In other convulsive and spasmodic diseases, more especially, spasmodic cough, occasional benefit has been derived from it, and favourable reports have been given of its action as a tonic and astringent in chronic catarrh. As an astringent, it is also not without use in chronic diarrhœa. Lastly, it is a favourite tonic with some, in various scaly cutaneous diseases, more especially lepra and psoriasis; in which it is usually given along with the solution of potash."

Nitrate of silver illustrates the second case—that of medicine undergoing changes in the canal, which render their absorption impossible. It is a drug which has puzzled physicians; knowing little about it, they thought it might do good in epilepsy; they found with it (as with every other drug that has been tried) that some patients improved and others got worse; and I am not aware that there was any particular reason for connecting either event with its action as a remedy. Heller, whom I have often quoted to you in this lecture, has inquired into the chemistry of this medicine in a number of cases, which I need not specify further, than to show to you that they were sound experiments; in one case ten grains, in another case twelve grains, were taken daily during a period of three months. Now, no trace of these large doses could be found, either in the blood or in the urine; and, on further inquiry, it was found that every particle of the drug was discharged with the feces in the form of chloride—that it had probably assumed that form on entering the stomach, and thence had passed on without change. This explains, why the internal use of nitrate of silver does not *always* make patients black, according to its well-known *occasional* effect; perhaps it would do so uniformly, if it were absorbed; but within the ordinary limits of a dose, this can hardly ever occur, nor, except in very rare instances, can the medicine be other than inert.*

We see something similar with iron, though happily not to the same extent; a very large proportion of each dose undergoes a change, which leads to its traversing the intestines in the unabsorbable and inert form of the insoluble sulphuret; and it is a comparatively small proportion which enters the circulation, and constitutes so invaluable an agent for promoting the development of the blood.

As a last hint in respect of humoral diseases, and the medicines which relieve them, I may tell you that there are instances in which some *excernendum* appears to be detained in the blood, for want of some other definite material with which it may combine for the purposes of discharge; and in which, if one knew exactly how to act, one might do good by adding the defective element. I can illustrate to you what I mean by a point in the history of delirium tremens;

* I cannot refrain from drawing attention to the foolish pretence of medical treatment, which consists in the exhibition of what are called *demulcent* preparations in various internal maladies, under the notion that, by reason of their original sliminess, they impart some peculiar bland and soothing quality to any prescribed secretion. It is especially in the complaints of mucous membranes that they have been prescribed—in gonorrhœa, in cystitis, in calculous disorders, in various inflammations of the intestinal canal, in bronchitis, and the like. In the prevailing impression that such materials act specifically on mucous membranes and shield them from acrid contact (as though additional animal mucus were laid afresh over the surface), it seems totally forgotten that these mucilaginous drinks, so soon as they enter the intestinal canal, undergo digestive changes, which divest them completely of the physical property, to which so much mistaken importance is attached. It may be very well for the laity to suppose that barley-water, or decoction of quince or mallow, can give direct and specific relief to bronchitis, or clap, in the manner here alluded to; but every competent physiologist knows, or ought to know, that no mucilaginous quality can survive the act of digestion; that these medicaments reach the organs on which they are supposed to operate in a form of absolute inertness as regards the pretended efficiency; and can diminish the acridity of a secretion (*e. g.* of the urine) merely by the water, which they furnish for its dilution.

begging you to observe, however, that I am not arguing for the humoral origin of the symptoms in that disease. Dr. Bence Jones drew attention, some years ago, to the striking deficiency of phosphates in the urine in this disease, and contrasted this peculiarity with an opposite one, of increase in those ingredients, in cases of true inflammatory action in the brain. In a case of the former description, treated at Vienna under Heller's observation, lime-water happened to be given as a remedy: the fixed salts of the urine immediately rose from a very low figure, 4.60 per 1000 to 13.2 (the phosphate of lime having increased nearly eight-fold), while the extractive matters fell from 22.66 to 10.1. In considering this case, it is difficult to avoid the conviction that the lime supplied a condition, which was previously absent, for the elimination—perhaps even for the formation, of other ingredients; and that the deficiency of phosphates must have been accidental, and secondary to that absent condition which the lime-water supplied.

I wish we had more information of this nature. I do not desire you to attach undue importance to the particular instance, but rather to consider it as a clue for inquiry into the obscure operations of other remedies, and into the means for treating humoral diseases. When we become enabled to deal preventively with these diseases—preventively, I mean, as regards their tendency to explosive attack—I doubt not that this power will consist in the application of measures acting during the latency of the disorder, in a manner analogous to that just indicated to you: it will consist in our constantly keeping the system supplied with means for eliminating that material (whatever it may be), which, by its retention in the blood, constitutes the latent stage, and prepares for the explosive attack of gout, rheumatism, carbuncle, and the like.

Gentlemen, in commencing this lecture, I did not disguise from you that the subject was obscure and unsatisfactory; that I could give you little certain information on much of it; that often I could afford you only hints and conjectures; that I must hope to render the consideration useful to you, mainly as the means of exciting your attention to the extreme deficiencies of our science, and inviting your industry to matters in which *exact observation* is so peculiarly required. Perhaps I have dispelled for you some pleasing illusions as to the omnipotence of drugs; but, believe me, it is infinitely to be desired that we should recognize the insufficiencies of our knowledge, and grapple with the difficulties of its increase, rather than voluntarily acquiesce in a system of sham therapeutics, and prolong the reign of a blind empiricism hostile to every interest of science and humanity.

LECTURE XII.

Morbid Poisons: their marked distinction from common poisons; generalization of their phenomena, constitutional and local; illustrated in case of continued fever. Pathology of infection, illustrated by inoculation of smallpox; immediate increase of poison; subsequent immunity of patient. What constitutes susceptibility to morbid poison? Peculiarities of syphilitic and vaccine infection. Mitigation of inoculated smallpox. Paludal poison: Cholera. Theories of infection: contagium animatum; illustrations of parasitic disease; their dissimilitude from phenomena produced by morbid poisons? Fermentation-theory; dissimilitude of the infective process from any known catalytic action. Origin of contagium in the blood? in which of its ingredients? Summary of results. Pathological principles of cure and prevention.

GENTLEMEN: The subject on which I have to address you to-day—the subject of Morbid Poisons, stands in very intimate relation to some of the matters touched on at our last meeting: partly because it furnishes additional illustration to the arguments which I then advanced, as to the general principles of humoral pathology; partly because it derives its own intelligibility from an application of those general principles.

The interest with which I now approach its consideration is much increased, as I remember that the most extensive observations and the profoundest reflections, hitherto published on the subject of morbid poisons, have emanated from this school. For, without going back to the days when Dr. Fordyce wrote his treatise on Fever (though it might indeed challenge comparison with any other production of the same date), I may remind you of Dr. Robert Williams's classical work, completed only nine years ago, when he was still physician to this hospital; and I may cite that work as occupying the highest rank in the practical literature of this country. I would earnestly recommend you to study his two volumes thoughtfully: you will rise from their perusal with an infinitely better knowledge of the subject than you are likely to obtain from other reading. You will regret that he no longer lives to teach here what he understood so well: a regret more than equally shared by those who had personal intercourse with him, and who remember with how much simplicity and kindliness of character his great professional attainments were combined.

In what follows, I may take for granted that you are familiar with the general phenomena of the diseases to which I have to allude. It would be far beyond my province to enumerate, in detail, what is distinctive in the symptoms and progress of the various fevers and allied disorders. I shall confine myself to a consideration of their specific causes, and of the manner in which these agents proceed to produce their characteristic effects; and I shall trace these effects only so far as they may help us to attain a knowledge of the relations subsisting between them and their alleged causes.

By *morbid poison* we understand a product, which is the supposed specific cause of certain specific diseases: of syphilis, for instance; of scarlatina, of typhus, of glanders, of smallpox, of hydrophobia, and the like;—a product, which has many striking differences from all other poisons, but chiefly these: first, that while other poisons (oxalic or hydrocyanic acid, or sulphuretted hydrogen gas) act directly in proportion to their dose, becoming more or less deadly in proportion as more or less of them is brought to bear on the organism; you may observe, contrariwise, that the *morbid* poison (the poison of contagion) produces its characteristic results, when given in the minutest conceivable doses, just as surely, and just as deadlily, as when the system is saturated with it: and, secondly, that while common poisons diminish from the body, or at the most remain stationary, during the production of their effects, morbid poisons apparently undergo, within the body on which they act, a striking and singular increase.

The phenomena which follow infection with a morbid poison consist of certain local changes, attended by a peculiar constitutional state. The *local* changes may be generalized as subacute inflammatory processes, attended (perhaps preceded) by the deposition of a *specific material*, which material in most cases contains an agent capable, by inoculation, of producing in another person the same symptoms as have attended its own generation in the original sufferer. The peculiar *constitutional* state is one essentially of depression; modified, no doubt, and intermixed with those phenomena of reaction which the living body (like a spring) always opposes to the direct pressure of exterior influences.

Of the local changes partaking of an inflammatory character, your memory can give you many illustrations: such are seen in the pustules of smallpox; in the cynanche and erythema, and kidney affection of scarlatina; in the intestinal ulcers of typhus; in the catarrh and eruption of measles; in the rupia or periostitis of syphilis; in the swollen parotid of mumps; in the dysentery of malarious fever; in the suppurating tumours of glanders; and in various other symptoms that might be quoted.

And, let me beg you to observe, it is because of these local differences in *effect* that we are impelled to distinguish the *causes*, and to speak of them as *specific:* syphilis never produces ulcers in the ileum, scarlatina never causes iritis; the causative poison of the one disease differs from the causative poison of the other, for on the selfsame subject it produces different effects.

Not so, or at least not remarkably so, with that constitutional state which precedes and accompanies the local changes. It represents what I have already sketched to you as generic features in the expression of humoral disease. Take, for instance, the incubative symptoms in a case of continued fever, and see to how many of the acuter blood-diseases the same description might apply. I purposely borrow the catalogue of symptoms from an impartial describer:*—"The expression of the patient's countenance alters; he becomes

* Dr. Watson—Lectures on Practice of Physic, under head of "Continued Fever."

pale, languid, and abstracted; those about him observe that he is looking very ill. He is feeble, and easily tired; reluctant to make any exertion of mind or body; listless, and often apprehensive of some impending evil. He loses his appetite; his tongue becomes white, and inclined to tremble; the bowels are irregular, often confined, sometimes affected with diarrhœa; his senses lose their natural delicacy. He has uneasiness or wandering pains in various parts of the body, and occasionally there is some giddiness; drowsiness, perhaps, during the day, and unsound, unrefreshing sleep at night. In one word, the patient *droops*. The regular onset of the fever is very frequently indeed marked by a shivering fit; another common phenomenon at the period of the invasion is severe headache......But you will also perceive, even when there have been no premonitory circumstances, that symptoms arise, even thus early, which belong to the nervous system, and denote some disturbance and alteration in the functions of sensation, thought, and voluntary motion. They are comprised under the general phrase, 'febrile oppression,' and they are different from what we notice when pyrexia or feverishness supervenes upon inflammation. The muscular power is sensibly enfeebled. Sometimes the patient will struggle against this, but in a few hours, or in a day or two at farthest, he takes to his bed."

Now, this sketch of the invasion of continued fever not only represents most accurately what it is meant to represent, but much more: with very slight modification, it is equally a picture of the commencement of erysipelas, of smallpox, or of scarlatina—in fact, of all the acuter infected diseases. And that which is characteristic of each individual poison—the determination, namely, of morbid products in one direction or another, arises only when the preliminary stage of depression has passed, and when augmented vascular action has set in; it belongs to the stage of reaction. A patient may die in the first access—in the first tremendous shock and depression of a morbid poison, almost as with a long draught of dissolved oxalic acid, or as with a dose of nicotine; and you may be absolutely unable to say, from any characteristic sign, what has killed him. Surrounding circumstances (such as the prevalence of a particular epidemic) may enable you to guess; but apart from such evidence, you could not say whether scarlatina, plague, smallpox, typhus, cholera, or yellow fever, had stricken the man down thus suddenly. Nor even in that partial and qualified reaction, which makes the second stage of fevers, would you be able to distinguish more certainly than in the first the nature of the poison, were it not for the admixture of symptoms derived from local changes. That the "patient is hot, flushed perhaps, and thirsty; that he has a frequent and hard pulse;" that his secretions (except under the special circumstances alluded to) are scanty and offensive; thus much belongs to all the cases equally. It is by the exanthema of one disease, by the peculiar delirium of another, by the evacuations of a third, by the dysphagia of a fourth, that you are able to say with what malady you are dealing. Your knowledge of its speciality depends on its *local* manifestations.

And now, gentlemen, to connect these striking phenomena with a cause, let me remind you of what takes place when you inoculate with smallpox. This will do as an instance of infection.

You receive, perhaps from a long distance, from Dublin or from Edinburgh, a lancet, on the point of which is a little dry animal matter. This lancet has pricked the pustule of a patient suffering with smallpox, and the contents of the pustule have been allowed to dry on the lancet. Now, with this lancet, you make a single puncture in the arm of a healthy person, not previously defended by vaccination or otherwise; and what results? "On the second day after the operation (says Dr. Gregory)* if the part be viewed with a lens, there appears an orange-coloured stain about the incision, and the surrounding skin seems contracted. On the following day a minute papular elevation of the skin is perceptible, which on the fourth day is transformed into a vesicle with a depressed centre. The patient perceives an itching in the part. On the sixth day some pain and stiffness are felt in the axilla, proving the absorption of the virus into the general mass of blood. Occasionally on the seventh, but oftener on the eighth day, rigors occur, accompanied sometimes with faintishness, sometimes with pain in the back, headache, or vomiting. The patient complains of a disagreeable taste in the mouth, and the breath is offensive, soon after which the eruption shows itself." If the patient have been a woman, and pregnant, her fœtus will generally have been affected, and if so, will have died. Finally, when the eruption has developed itself, you find that every one of these new pustules inherits the infective power of that from which they were developed; and thus from one patient you can obtain enough of the morbid poison to diffuse smallpox throughout the habitable globe in an inconceivably short space of time. Observe this immense increase of material; remember the almost imperceptible stain on the original lancet; here you have its material reproduced by a thousand-fold—a million-fold multiplication.

But it is not only by inoculation—*i. e.*, by breach of surface, that the disease can propagate itself to the body of a previously healthy person. As I have already stated, the fœtus in utero may contract the disease from its mother; therefore, the material cause of the phenomena is *soluble;* for between the circulating systems of mother and child there can be no other communication than by fluid matters. And further, the material is *volatile;* for persons having no contact with the patient, either directly or (except for the atmosphere) indirectly, are likewise liable to contract the disease.

There is yet another very striking point in the case. Your patient having recovered, suppose you try to infect him again in the course of a few months. You charge your lancet; you make the puncture as before; or you make half a dozen; you accumulate all means of infection about the subject of your experiment; but no longer will he give a single sign of the specific affection. You have

* Cyclopædia of Practical Medicine, art. *Smallpox.*

got from him all the phenomena he can give in answer to that particular reagent. I may compare his change of condition to this: suppose you had a tumblerfull of a solution of carbonate of soda, and added an excess of nitric acid; you would get vehement effervescence, more or less, according to the abundance of your dissolved carbonate, and continuing till it had effected the complete disengagement of the gas: then—that particular moment having passed, you might add nitric acid *ad infinitum*, but not another bubble would rise. Just so, your patient refuses to *effervesce* any more from new infection; certainly for a long time; perhaps for the rest of his life. You reapply the same cause as produced the phenomena before—identically the same material; and you get a different result. This fact conclusively proves that a change has occurred in the subject of your experiment; *a change in him* has altered his relations to an *unchanged exterior cause;* by this personal change the poison is rendered inert to him, while it retains its activity towards others.

We have it accordingly demonstrated, that for the production of the disease there must be a *specific internal*, as well as a *specific external* condition; that the former is liable to be exhausted; and, as it becomes exhausted in the production of material phenomena (namely, in the generation of pustules) therefore, obviously, it must itself be a *something material*, like that outward condition with which it co-operates; as the *poison of smallpox* is a something material and tangible, so the *susceptibility to smallpox* is a something material and tangible. Of this material—whatever it may be, no trace remains in the blood, when the disease has completed its course.

Thus we get a general formula for the pathology of smallpox, which will be useful as a standard of comparison for the other poisons in our list. A certain organic material, A, soluble and partially volatile, affects particular relations with B, an ingredient (apparently a normal ingredient) of the blood: the result of their coming together are (1) the utter destruction of the latter, B; and (2) the immense increase of the former, A; not, indeed, at the spot of infection, but elsewhere. On the one hand, the *virus* augments so much that it is found all over the body, forming innumerable pustules, and contaminating the breath with its volatile miasma; on the other hand, the inward natural *ingredient of the blood* simultaneously diminishes, and at the end of the process is found totally exhausted.

Look at this as a chemical experiment: you add A to B; presently you find that B has vanished, and that A has undergone an immense augmentation. What is the meaning of this? What has become of B? Whence has the new A been derived? It is difficult to avoid the conviction, which arises with almost logical certainty, that the increase of one material and the decrease of the other, have stood in essential mutual relation; that, in short, it has been a process of *conversion;* that the essential relation of the two matters (that derived from *without*, and that contained *within*, the blood)

has consisted in the ready convertibility of one into the other; that the specific power of the virus is its power of effecting this transformation, and no other.

Finally, that material of the blood in which the virus of smallpox effects this peculiar change, seems, though a *normal* constituent, to be no *essential* one; for the patient, convalescent from smallpox, though with no demonstrable trace of that constituent in his blood, returns to at least as good health as he ever enjoyed previously. It may be added, too, that, in a certain very small proportion of persons, this natural ingredient of the blood appears to be not *uniformly* present; for there are persons (apparently undefended by any previous occurrence of the disease, or by other known means) in whom your original inoculation would have failed; persons, who would have shown a non-infectibility by the poison, and who, therefore, must (at least for the time) have been without that material in their blood which constitutes the susceptibility to the disease.

The line of argument which I have followed in regard of smallpox, leads to very similar, though not identical results in respect of measles, scarlatina, typhus, glanders, plague, and probably hooping-cough: there is the same evidence that a certain definable state of the blood is one of two conditions for the formation of the disease: that this preparatory and permissive state (different and characteristic for each separate infected disease) is a peculiar chemical state, dependent on the presence, or the excess, in the blood of a material *convertible into identity with the poison:* that the poison, thus augmented, endeavours to eliminate itself by surfaces, the choice of which is a distinctive and specific mark of each poison respectively: that, for a greater or less time after the fulfilment of this eliminative process, the susceptibility to the disease is exhausted: and, finally, that the severity of the disease, in each instance, will depend—not on exterior circumstances, but on interior and personal conditions; not on any variation in the degree or amount of foreign infection (so long only as this has actually occurred) but on the patient's own possession, within the stream of his circulation, of a larger or less abundance of that specific material, which—as I have argued—constitutes, on the one hand, his susceptibility to infection, and, on the other, his power of expressing the disease. He must necessarily evolve symptoms in proportion to his richness in that which furnishes their material.

In the poisons of these diseases great difference of volatility is observed: those of syphilis, plague, hydrophobia, and glanders may be considered absolutely fixed. There is difference also in respect of elimination; some of the poisons determine themselves exclusively to surfaces by which they may be discharged; but others—as, for instance, hooping-cough, and perhaps hydrophobia—have not this tendency in so marked a degree. The local determination most characteristic of hooping-cough, seems directed chiefly to the nervous centre of the pneumogastric: with hydrophobia it is more difficult

to speak positively, for the disease proves fatal too soon for the local determinations to have clearly expressed themselves.

But there is a very common disease, which introduces some new difficulties into the doctrine of infection. I mean syphilis. If you inoculate with syphilis (I mean, with the secretion of a chancre or a bubo,) you get, almost certainly, a pustule at the spot, rapidly followed by induration, and by a considerable local increase of the poison. For wherever that induration extends, there you have the characteristic infective material of the disease. But presently that induration softens itself; the ulcer which was seated on it becomes cicatrized, and the patient flatters himself with the conviction of recovery. Six weeks afterwards, more or less, that conviction begins to be disturbed: some general indisposition attacks the patient; not quite such as I described after the inoculation of smallpox, not so acute or severe; but a feeling of being out of sorts, and a general feverishness and *malaise* (sometimes very marked and noticeable, sometimes less so) in the midst of which appears the characteristic exanthema of secondary syphilis, often with sore-throat, and presently with various other local inconveniences, admitting of comparison with those consequences of morbid poisons at which we have already glanced. But there are two very striking peculiarities in the history of syphilis: first, these secondary discharges—the pustules or bullæ on the skin, the ulcer in the throat, or any other eliminative sores opened by the disease—these do not contain a virus similar to that of the original chancre. From the secondary pustule of smallpox you get (as I have said) identically the same virus as from the original pustule; but from the secondary sores of this other pox, you do not. The poison of secondary syphilis is different from that of primary syphilis in this respect, and likewise in another: the poison of primary syphilis is insoluble; it will not act through a continuous membrane; the poison of secondary syphilis, on the contrary, is soluble, and acts (as we see in its affection of the fœtus in utero) through the unbroken walls of capillary bloodvessels. And a second point of peculiarity in the disease is—that it does not exhaust, nor (so far as we know) materially diminish the patient's susceptibility to future infection. Accordingly, the general description of the *modus operandi* of the primary syphilitic poison seems to be this: being inoculated, it acts to a certain extent like those which we have already considered, converting into its own likeness those appropriate materials of the blood which come into contact with it;* but this action is apparently limited, and at last arrested and reversed, by a disposition inherent in the virus to enter into some new union, or to reciprocate some

* It is interesting to observe that, whatever change syphilitic inoculation effects in the blastema of a part, that change is apt to repeat itself in the adjoining lymph-glands. The multiplied poison does not assume its *secondary* characters in them; it still retains its *primary* peculiarities, and may (*e. g.*, from an ordinary bubo) be communicated by inoculation. The affection of the lymph-glands by primary syphilis adds a further illustration to some remarks made in a former lecture (that on Cancer) as to the transferability of disease in these organs by *continuity of blastema.*

new modification with other ingredients of the blood; by which union or modification it attains a second form, wherein (whether by addition or by subtraction of matter) it comes to possess new qualities;—*solubility* which it had not before, and an *inability to propagate itself by inoculation* from the surfaces at which (judging by analogy) we may suppose that it discharges itself. In becoming a true blood-disease it ceases to be communicable except by what is equivalent to transfusion of blood.

The action of the vaccine virus shows a somewhat similar peculiarity. Vaccination leads to a local multiplication of the poison; and we are therefore justified in arguing analogically, that there exists in the blood a material convertible into vaccine virus. But here (as with syphilis) the blood-material, in the act of its conversion to virus, seems capable of some new metamorphoses or combination, which renders it inert, or leads to its removal from the system. We have good grounds for supposing that this blood-material is identical with that which constitutes the susceptibility to smallpox: so that its inertness, or its removal (artificially effected by vaccination) confers on the patient the same immunity as we would gain from having the material exhausted (in its natural manner) by an attack of smallpox. The difference in the intermediate steps is striking: inoculate with smallpox, and the blood-material converts itself into virus—not at the puncture only, but elsewhere, and leads to the formation of pustules over the whole tegumentary surface of the body: inoculate with vaccine matter, and the same material converts itself into virus also, but into a virus so liable to change by some other ingredient of the blood, that, as fast as it rises, it becomes neutralized, or excreted; and this in a manner so silent and imperceptible, that—except for the momentous change effected in the patient's blood by the destruction of that which constituted his variolous susceptibility, we might almost overlook the constitutional largeness of its operation.

I may take this opportunity of explaining to you a difficulty which arises in the doctrine of morbid poisons, from considering the mitigation which their severity often appears to undergo, when they are infected by artificial inoculation. It appears, that while infection is the certain test and evidence of certain materials in the blood, inoculation is, in many cases, a much finer test than can be afforded by atmospheric inhalation; and, as the severity of symptoms will be in proportion to that chemical state of the individual by which he is infectible, so I would explain the frequent comparative mildness of inoculated smallpox. By inhalation of the volatile virus, fewer would be affected, but those few would have the disease severely; this method of infection including only those persons who possess a great abundance of the material which renders infection possible, and who (by reason of their large possession of that material which leads to the production of symptoms) would naturally suffer much; while the process of inoculation (being, as I expressed it, a finer test) will elicit evidence of the disease from a far larger number of persons, will include many who possess a

minimum of the symptom-producing material, and who, for that very reason, will suffer the disease in its mildest form. On the same principle, I would explain that other fact, well known in practice, that on the first invasion of an epidemic, the proportional mortality is greatest; while later in its progress (when far larger numbers are attacked) the proportion of recovery is increased. At the commencement of the epidemic, the exterior causative influence is at its minimum; those only contract the disease at this period who possess in an extreme degree, that interior condition which constitutes the specific susceptibility, and which (as I have already explained) measures the severity of an attack in exact proportion to the facility with which it is incurred.

With respect to that well-marked deleterious agent, which arises in the decomposition of vegetable matter—the *paludal poison*—the poison which is the cause of the various intermittent and remittent diseases, from the milder ague of our climate to the deadly malarious fever of the tropics—I may confess that I hardly know whether it ought to be classed with the *morbid* poisons now under consideration, or perhaps rather with the *common* poisons derived from unanimated nature; for if it differs (as no doubt it does) from these latter poisons, in its longer period of latency,* and in the slowly progressive character of the functional and textural changes which it works in the body; on the other hand, it may be argued that these are minor points of difference, and that in more essential respects the paludal poison deserves to be accounted a common one. Where intense, it spares very few, and therefore cannot be proved to have those special affinities in the blood which belong to the morbid poisons: it confers no subsequent immunity, and on this account also cannot be thought to have such relations: it acts in proportion to its dose, which is not the case with morbid poisons; the circumstances rendering it severe are local (as opposed to personal) circumstances; for in certain countries it is always immeasurably severer than in others; and lastly, but, as I think, most importantly, it does not reproduce or multiply itself in the human body; it cannot convert any element of the blood into its own similitude; nor are its effects capable of propagation from one person to another.

That it is a *material* poison, capable of effecting entry into the

* "The period of time that the paludal poison may lie latent varies from a few hours to ten or even twelve months. Our troops during the Walcheren expedition suffered immensely from intermittent and remittent fever. On their return, however, to this country, great care was taken to quarter them in situations remote from all known sources of marsh miasmata; yet fresh cases continued to occur as late as five, six, eight, nine, and even ten months afterwards. A knowledge of the distant period the paludal poison may lie latent explains many facts otherwise of difficult solution. We are perpetually, for instance, receiving into our hospitals, both in winter and early in the spring, patients labouring under intermittent fever—seasons when the temperature of the atmosphere is so low as to render vegetable decomposition almost impossible. It seems probable, therefore, that the vernal intermittent must result from marsh-miasmata, received into the system during the preceding summer or autumn, and which has remained dormant in the system till some predisposing circumstance has roused it into action."—*Williams*, ii. 465.

blood, and not any mere physical influence inherent in the soil, seems certain: we can trace its operation in a definite line of progress through space, and can observe it becoming arrested by material impediments—by trees, or by a line of buildings; it is soluble, too, for it has been known to affect the fœtus in utero; and moreover, it has difficulty in crossing water—probably from undergoing solution there; heat is its great evolver; watery moisture its chief vehicle. Whether it consists in some complicated organic product, or is of a simpler constitution, I am unable to decide. I incline to the former supposition; but I may tell you that the late Professor Daniell,* in analyzing the deadly waters of the Gambia, found in them no unnatural quality but one—they contained a considerable quantity of sulphuretted hydrogen.

The severer operation of the paludal poison often illustrates, what is true of all poisons acting through the blood, that life may be extinguished by them without evident structural lesions remaining. Dysentery, disease of liver, spleen, or peritoneum, and the like, arise under minor degrees, and slower operation of the poison. Yellow fever may kill in a few hours, leaving no posthumous sign of local determination. Time will not allow me to enlarge on the symptomatology of malarious diseases. For the sake of our subject generally, I would merely suggest two points for your consideration—first, that the characteristic remission and recurrence of symptoms in this class of disorders may depend on the alternate exhaustion and reproduction, either of the poison itself, or of that blood-material on which it acts; secondly, that their marked tendency to affect the spleen with chronic enlargement and inflammation is a peculiarity to which I shall presently again advert, as it suggests some explanation of what is special in the disease.

In intimate, but most obscure relation to these paludal poisons, stands the unknown cause of the so-called Asiatic cholera—an influence which is migratory, moving in definable procession round the globe, and affecting large regions in succession, but yet, in its migrations, evincing so singular a preference for malarious districts, that it might be called *epichorial* rather than *epidemic;* and we might, not improbably, conjecture of its wandering cause, that it consists in some agent capable of determining a secondary modification in whatever malarious atmosphere it may traverse. Whether the primary influence be aerial, telluric, or even astral, we are quite ignorant; we only know, that in some parts of Asia it is now constant, and that periodically it tends for a while to enlarge the area of its operation, advancing with each year more and more, till its shadow encircles the globe, and then retreating again within its original focus. In its European excursions, it has prevailed for three years, recurring each autumn in the localities first affected by it, with a severity gradual, both as to its increase and its decline. Of its communicability from person to person, proof has never yet been

* Exception has been taken to this statement of Mr. Daniell's, I think by Dr. McWilliam, in his account of the Niger Expedition. The symptoms of intermittent and remittent fever are certainly not such as would be produced by sulphuretted hydrogen.

given; but of the intensely poisoned condition of the district in which it prevails, innumerable records bear evidence. In all probability, the disease spreads independently of any personal intercourse; and the power of infection may be considered an appurtenance of the district rather than a property of the sufferers. The eliminative acts excited by the poison of cholera are among the most violent manifestations of disease, stripping off the epithelium of the intestinal canal, and purging forth fluid by stool and vomit, with a rapidity which literally *desiccates* and shrivels the patient, so that his blood, by reason of its extreme inspissation, is rendered incapable of its normal functions. There is a degree of its operation, however, in which the choleraic poison, like that of yellow fever, may kill and leave no sign. Death may occur from its intensest action, even within a few minutes. When the cholera reached Muscat (says Dr. Williams), in some instances only ten minutes elapsed from the first seizure before life was extinct; and at Punderpore, the disease is said to have raged with such severity, that 350 persons died in the streets, "tumbling over each other lifeless," or, according to another authority, as if "knocked down dead by lightning." I need hardly tell you, that in such cases no eliminative actions could be established, nor would any characteristic morbid appearance be found in the solid organs of the body.

And now, Gentlemen, to return to the truly morbid poisons (for I do not include the paludal poison in this phrase, except where I distinctly mention it)—I have spoken with some decision of two conditions as necessary to the infection of disease—first, of course, the existence of the poison; secondly, the existence of some other substance, an ingredient of the blood, over which the poison exercises a peculiar, usually an unique influence. I do not consider this statement to embody any particle of theory: I consider it to be the simplest generalization of facts which lie within the sphere of your daily observation.

But you will probably expect me to give you more exact information as to that mysterious causative agent which constitutes the power of infection; you will probably expect me to tell you what it is, and how it operates.

This is no easy task. To explain the nature of a cause, which, in the act of its operation, undergoes, as it seems, spontaneously, an almost infinite multiplication of its causative principle, and which yet, *ipso facto*, ceases to be causative in the original sphere of its operation; this cannot but be considered a most intricate pathological problem.

The immense multiplication of the poison (as I have illustrated it to you in smallpox or measles) is at once an almost overwhelming difficulty. What is there like it in chemistry or in physics, or in any operation of brute matter on the living body? The difficulties arising in this point are so great, that some very able pathologists have addressed themselves to the labour of explanation. I may confess to you that, to my mind, none of the attemps hitherto made appear to have been successful; but I will tell you the two opinions

which at present chiefly prevail, and I will explain to you what I conceive to be their deficiencies and errors.

Partly by reason of the regenerative power of the poison, and partly to overcome difficulties which arise in the question from considering the migration of epidemic diseases, Dr. Holland and Professor Henle have ingeniously conjectured, and with great knowledge of the subject have argued, that perhaps the essence of a morbid poison might be a living thing; that the poison might be *contagium animatum;* that fever and the allied disorders might be consequences of a parasitic development in the body. Thus would be explained —thought these writers—the latency of diseases after infection, the spread of epidemics, and the reproduction of the poison within an infected organism.

Dr. Holland's interesting essay is entitled, "The Hypothesis of Insect Life as a cause of Disease." I presume that he attaches no particular importance to the word *insect;* that he means *animalcular life;* only using *insect* as synonymous with *animalcule.* So, in discussing these theories, I shall not attend to the special distinction between insect and animalcule, but shall examine them briefly together, as the *parasite-theory of fever.*

I find the utmost difficulty in accepting this theory as a sufficient explanation of the fact. If you examine parasitic diseases from first to last, you will find that they are, perhaps of all known maladies, the most essentially local. They may be very extensively diffused—may be in very many spots of the body—and the sum total of many small local irritations may be a large general irritation; or, if the parasites are large as well as numerous, they may drain the system of blood, and may anæmiate and kill the animal, as we see in the rot of sheep; but all we know of parasitic influence on the health (and I may observe that a good deal is known)—all, I say, is referable to these two heads: *local* inconvenience from pressure or from irritation; *general* inconvenience, either febricular —from that local irritation becoming inflammatory, or anæmiative —by draining and impoverishment of the blood. Both in the lower animals and in man, we are familiar with very many instances of parasitic disease: in addition to the well-known cases of scabies, hydatids, intestinal worms, and the like, where the cause of disease is an animal parasite, there are others in which vegetable growth occurs parasitically on the living body. Various forms of scabby porrigo have been shown to depend on parasitic vegetables—mycodermata; and within the last two or three years a new instance has been discovered—a peculiar torula developed within the hair in cases of *porrigo decalvans,* as the cause of baldness without coexisting disease of the skin. Not only the animal kingdom suffers from the parasitic invasion of these low forms of growth; vegetable organisms likewise have their epiphytic parasites; and to an extent of which animal pathology furnishes no measure. Their blights are epidemic. The minute fungi which constitute such diseases, multiply with incredible rapidity; "frequently (says Sir Joseph Banks, in his paper on the Blight of Corn) in the latter end of the

summer, must the air be loaded, as it were, with this animated dust, ready whenever a gentle breeze, accompanied with humidity, shall give the signal, to intrude itself into the pores of thousands of acres of corn." Now here is exactly the case for the vegetables that Henle and Dr. Holland imagine for animals; and what is the result? Why, wherever on the plant they may alight, a *local* result; a result so like the porrigo of animals, that a distinguished botanist calls these diseases the *exanthemata* of plants. In each pore, where a sporule alights, it grows, and branches, and breeds—spoils the part; and, if there be enough of them for the purpose, then (like hydatids in the sheep) they drain and starve the whole organism of the plant. I can give you a good illustration of this simple method of operation, in quoting one paragraph from Sir Joseph Banks's paper, which I have already alluded to. He remarks that, "although the seeds of wheat are rendered, by the exhausting power of the fungus, so lean and shrivelled, that scarce any flour fit for the manufacture of bread can be obtained by grinding them, these very seeds will (except, perhaps, in the very worst cases) answer the purposes of seed-corn as well as the fairest and plumpest sample that can be obtained." This is very unlike syphilis or smallpox: they produce on the organism an influence utterly unlike these phenomena of *starvation;* nor is the mother's disorder, by these poisons, such as to leave her offspring uncontaminated. As a somewhat analogous case occurring in the animal kingdom—analogous, I mean, as to the abundance of parasitic life undergoing development and effecting change in the body—I may remind you of that immense diffusion of parasitic eggs which I told you I had seen in rabbits, not only loading their livers, but filling even the follicles of the intestine like epithelium; and yet with no general affection of health.

But there is one case, still more nearly analogous to vegetable blight, which Henle puts foremost in his argument, and to which he attaches great importance. In the silk-making parts of France and Italy, a disease has been noticed to rise like a pestilence among the worms, to kill them by myriads, shrivelling them into dry corpses within a very short time of the attack. This is unquestionably a parasitic disease, and it is eminently infectious. A white efflorescence appears on the dead body of a victim of the disease soon after death, and increases, until at last efflorescence has taken the place of the body: the body has gone, and a heap of mould is in its place. If inoculation be made of some of this white material into the body of a healthy worm, in six days it will be manifestly ill; in seven, it will be dead; in ten or twelve, it will be reduced, like its predecessor, to a mere heap of cryptogamic vegetation. The researches of Audouin have shown that, during life, this vegetation had been rapidly advancing in the interior of the animal, diffusing itself wider and wider from the spot of inoculation; and we have every reason to suppose that the changes which occur are only such as I have stated to be the general results of parasitic growth, developing itself at the *quantitative* expense of the animal,

killing it only as the *extreme* result of its mechanical pressure or exhaustive drain—choking it or starving it.

See, then, how great is the difference between these phenomena and those of the morbid poisons to which they are compared: an animal invaded by parasites dies only when, in an ostensible mass, they occupy the space or the nutriment of its body. Their effects on life are in direct proportion to their manifestness in parts. The severest operation of morbid poisons, on the contrary, leaves no trace: local disorganization or detriment, instead of having advanced to its utmost possibility, will not even have commenced. Therefore, as respects the poisoned condition of a patient, with cholera, plague, or scarlatina, I find that its phenomena bear no similarity whatever to that of a sheep perishing with rot, or a silkworm with muscardine; it is anything rather than death arising in the encroachments of local disease.

Perhaps, Gentlemen, you will think I have kept my best argument for the last, when I tell you that observation has shown no parasitic formation in connection with the diseases under our notice. Take a piece of smallpox skin, or scarlet-fever kidney, or syphilitic periosteum—do you find it occupied by parasitic development, animal or vegetable? Certainly not.

Briefly stated, then, the argument stands thus; symptoms are absent, which parasites—if injurious—would unfailingly produce; symptoms are present, which parasites, however injurious, could not produce; and, thirdly, the parasites themselves elude discovery.

In rivalry with the parasite-doctrine of morbid poisons, it has been attempted to establish a *chemical* theory. You may have gathered from various parts of my present lecture, that I consider the phenomena of infective diseases to be essentially chemical, and that I look to chemistry to enlighten the darkness of their pathology. *Qualitative modifications*, affecting the molecules of matter as to their modes of action and reaction, are such as form the subject of chemical science; and those humoral changes which arise as the result of infection clearly fall within the terms of its definition. Unfortunately this view of the subject has been little cultivated; it has not had the advantage of being explored by any competent pathologist; the crude and inaccurate manner in which Professor Liebig advanced his so-called theories of disease having rather tended to alarm all cultivators of exact observation, lest their domain should once more be swamped in some flood of pseudo-chemical fancies. "Nothing (thinks Professor Liebig) can be simpler than this very large question. The morbid-poison changes in the blood are fermentative; just such as occur in beer-making. The morbid poison, acting as ferment, may be any organic matter in a state of change. The blood represents the sweet-wort. The multiplication of the poison is analogous to the increase of yeast in fermenting liquors; and as this latter increase is contingent on the presence of gluten in the saccharine solution, so the former increase is dependent on the presence in the blood of some specific substance admitting of transformation." To the laity this may sound simple and

satisfactory: for the word *fermentation* in chemistry (like *hysteria* in medicine, and *sympathy* in physiology) may be made to signify anything or nothing. The doctrine of a humoral fermentation—of a "concoction of the juices" produced by some exterior infectant—this, as a vague and general theory of fever, has prevailed, I may almost say, from the days of Hippocrates to our own. If Liebig uses the word *fermentation* to mean no more than it might have meant some centuries ago; if he means merely that in the blood a change (of which he knows nothing definite) occurs by reason of some exterior influence (of which likewise he knows nothing definite), and leads to certain eliminative acts (of which, thirdly, he knows nothing definite), I see no reason to combat these very unobjectionable positions. But if he, as a chemist, whom one supposes to be accurately informed on the exact phenomena of fermentation, really believes that the cases are parallel, and that the changes effected by a morbid poison are similar (except in the most popular sense of similarity) to those of alcoholic fermentation, he is quite at fault; as the practical men of one science are very apt to be, when they extemporize theories for some other department of observation.

I think it important that you should examine this matter thoroughly; that you should not rest satisfied with a mere figurative phrase; but should learn the essential differences which subsist between the fever-process and its pretended analogue. You will observe that, in the fermentation-theory of fever, Liebig compares the increase of the morbid poison to the increase of ferment in the development of alcohol. Now here at once is a flaw in the argument. The ferment (with one single exception) does not increase: and Liebig deals only with the exception. Among the infinite number of such agents, there is certainly one ferment which increases —yeast. And why? Because it is an organized vegetable production—and because the chemical changes attending its vital growth are, in the particular case where it is employed, the fermenting influence. But, as you know, the fermenting process may be provoked by many other chemical changes than this; throw into your saccharine solution a lump of decomposing animal matter, or pour urine into it, you get fermentation with great certainty—but, I need hardly tell you, with no increase of the animal matter or of the urine employed. The real influence which sets off the fermenting process in a liquor susceptible of it is the introduction of something in a state of chemical change; it may be the change of putrefaction in the matter introduced, or it may be the change of growth; either equally will answer the purpose; the brewer might dispense with yeast (though probably his customers would prefer that ferment to some I have mentioned), but in no other case would there be any increase of ferment. The increase of the ferment is quite accidental in true fermentation, occurring only when (as in the use of yeast) some living growth is employed as the instigator of chemical change. And I may observe incidentally, that this one case of fermentation by growth (the only one in which the ferment increases) is singularly incomparable to infective blood-diseases: seeing that a process of growth is incessantly advancing within the

stream of the circulation; and if the act of growth (as such), occurring in this plasma of the blood, could effect fever-changes there, we should never be without influences sufficient for its production; never, unless we could arrest the development of our blood-corpuscles. Here, too, I may add that, in order to test this fermentability of the blood, I have repeatedly performed experiments by introducing within the circulation materials in the fullest activity of chemical change, not putrefactive: saccharine solutions in which yeast was vegetating: starch in act of undergoing conversion to sugar by the action of diastase: solutions of pepsin: pulp of growing animal tissue: and I have not, on any single occasion, seen a result ever so little like the progress of infective disease, or like fermentation of the blood, produced by these injections.

Further, according to Liebig's view, if there be present in the blood a certain matter analogous to gluten in the vegetable infusion—a matter having some certain relation to the exterior poison of the disease; if both yeast and gluten, as it were, are present in the blood, then fermentation occurs in the total fluid, and gives origin to the symptoms of fever. You will observe that on this supposition all morbid poisons would lead (though by different routes) to that one fermentation; and therefore, as all fermentation of sugar gives alcohol and carbonic acid, so ought all fermentation of blood to give uniform products; the infection of smallpox, typhus, and scarlatina ought ultimately to produce the same results. But, without dwelling on this, let us at once ask, what evidence is there of this fermentation of the blood? Surely a great chemist must attach definite signification to the word, and must mean to denote by it some total change of the properties of the fluid—not perhaps that it shall become beer, but that it shall become something very different from blood. Such total change has never been observed, nor anything approaching it. I know of no humoral changes characteristic of infective diseases beyond those I have already alluded to—changes, moreover, not chemically observed, but physiologically inferred, and confined (so far as we know) within limits which are partial and specific for each particular disease.

The peculiarities which Liebig appears to have completely overlooked, in his attempt to explain the operation of morbid poisons, are these: (1) that the agents in question are very various, affecting different ingredients of the blood severally and distinctively; (2) that their sphere of action in the blood is very partial, nowise extending, beyond the particular ingredients which they respectively affect, to an entire decomposition or "fermentation" of the blood; (3) that the increase of the poison, coinciding with the decrease of the affected material in the blood, and consisting almost certainly in the conversion of that material, has not any true analogue in the fermentative process.

The phenomena of infected diseases appear then, in many respects, to be *sui generis*. Certainly they are chemical. Probably they belong to that *class* of chemical actions called catalytic; where chemical combinations are modified by the presence of a body,

which itself either remains unchanged, or at least does not enter into those new combinations determined by its contact; as when, for instance, platinum determines the union of oxygen and hydrogen, without any change of its own, or when oxalic acid occasions the decomposition of oxamide, or diastase the conversion of starch, or yeast the fermentation of sugar. Probably, I say, they may belong to this *class* of operations—a class already most heterogeneous; but in this class, if referred to it, they would unquestionably constitute a new species; for among the instances which I have cited, and among all that are known of analogous action, there is none which accurately corresponds to the operation under our notice. If, therefore, for convenience of phrase, we speak of the action of morbid poisons as a *catalytic* process; and if (with the Registrar-General) we speak of the numerous diseases excited by these poisons as *zymotic* diseases, it must be with a distinct recognition that for such nomenclature we have extended the former application of the words, and have not demonstrated the identity of our organic processes with those chemical actions previously expressed by them. With time, and with riper knowledge on the subject, this caution may become unnecessary. Meanwhile, in employing such phrases, be careful to remember that, however suggestive they may be as generic terms for acts having a certain obscure analogy, they do not include any explanation of the processes which they denote.

From these remarks on the general nature of the infective process, I proceed to consider the material which determines its occurrence. What this material—the principle of infective disorders in the human subject—may originally have been, we are totally unable to say; but, whatever may have been its first method of generation, we can now confidently speak of it as a possible product of the human body; we know that it is liable to develop itself out of some constituent of the human blood.

What are these constituents? Observation and argument sufficiently show, that the blood-corpuscles* and albumen can hardly be the constituents in question: first, because, after death by zymotic disease, they are found without evident alteration, and no considerable change in them could escape notice; secondly, because they are indispensable to life, and their even temporary transformation (if complete) would of necessity be fatal; thirdly, because immunity could never be attained by one attack of any particular disease, if it were requisite to exhaust these products: re-exposure to infection would insure a return of the disease and a re-appearance of its phenomena.

For somewhat similar reasons, we may conclude that the salts

* There are some reasons for doubting whether the paludal poison may not perhaps act on the blood-corpuscles: some of the symptoms of yellow fever, and the notorious tendency of ague to produce secondary affections of the spleen, seem, though indistinctly, to point in this direction. But I confine myself in the text to diseases of animal infection, which, alone, are attended with conversion and exhaustion of materials proper to the blood. The vegetable poison of ague might, perhaps, act slowly and partially on the corpuscles of the blood; but none of the ordinary animal zymotics could do so without betraying their action, in the manner stated above.

are not the elements concerned. Fibrin and the so-called extractive matters are what remain—can these be the ingredients in question? Substituting for the chemical phrase "extractive matters" the physiological one "waste of the tissues," I am strongly disposed to think an affirmative answer to that question; or, at all events, unhesitatingly to point here as the direction in which accurate pathological investigation may be made with most prospect of success.

For, in the first place, they are matters already in progress of decay, and therefore eminently susceptible of new modification; in the second place, they are inessential to the nutritive processes, and that removal of them from the system, which would give immunity from reinfection, might be accomplished without withdrawing a vital ingredient from the blood; in the third place, only of such matters as these can it be said that some of them occur but once in life. In infancy, in early age, and till puberty, there are certain waste materials which never afterwards occur; the temporary cartilages have to waste away, the thymus gland has to decay, peculiar changes referable to the sexual system have to be accomplished, and the effete products of these changes have to be eliminated from the system. And fourthly, notice that the surfaces and organs most prone to affection in the diseases under consideration are those which are eliminative and defecating; those whose normal products can hardly be retained for any time within the body, much less out of it, without undergoing a fetid decomposition, which sufficiently stamps them with an excrementitious character. Bowels, skin, kidney, tonsils, are the favourite resorts of the several fever-poisons, just as they are the surfaces by which naturally the organic waste of the several tissues is eliminated. And it may not be amiss to notice that, whereas the normal and healthy discharge of these substances commonly tends to occur in the highest attainable form of oxidation; and whereas, under a variety of atmospheric circumstances interfering with their efficient oxidation, they must tend to accumulate in forms more susceptible of fetid decomposition; so it is peculiarly under such circumstances—where ventilation is defective—where human beings are unduly crowded—where the air is loaded with deoxidizing influences—that zymotic diseases tend to affect the system, either through a new generation of their poison, or through some vast increase of susceptibility thus engendered.

On inquiry, it might appear that the relations of infective material to these natural products are definite and constant; that one—let us, for instance, say syphilis—would stand in the particular relation to fibrin; it would be obvious that such an one would be of almost universal inoculativeness, and could only for a very short time, if at all, exhaust the patient's susceptibility to reinfection; and that a drug having certain relations to fibrin (mercury, for example) would interfere with the affinities established by the disease. It might appear that another material, having its origin in the organic waste of nervous substance, would constitute the liability—say, to typhus; such an origin would almost fix the circumstances increasing our proneness to that disease, as well as prefigure the

symptoms attending it. Of another material it might appear that it originates in the infantile decay of temporary cartilage, or of thymus, a decay occurring only once in life; that such material would constitute the susceptibility to measles or hooping-cough, a single attack of which commonly exhausts the patient's susceptibility for ever. Of a fourth material it might appear that it arises in those changes of blood which attend the inflammatory and reparative processes, under direct atmospheric influence (as in open wounds, cutaneous or mucous), and that in such a product would consist the humoral liability to erysipelatous infection, and to puerperal fever. I need not multiply these hypothetical cases, but, before leaving them, let me beg you to understand that I employ them only as *illustrations;* that I do not adduce them as pictures of what occurs, only as diagrams explanatory of my meaning.

That the specific materials of the several morbid poisons, as they now pass daily under our notice, constituting the principles of zymotic infection, are either actually derived from the blood, or might have been thus derived, is quite a certainty. Whether each of them, in its first and original derivation, was a native ingredient of the blood, identical with that on which we now see its influence exerted; and whether its first conversion into a specific *materies morbi* occurred without exterior infection, are points which cannot be decided with confidence. In respect of many infected diseases, however, this view of their having first of all arisen spontaneously, would seem consistent with analogy. Experience confirms this theoretical view; for we not unfrequently hear of an outbreak of smallpox or scarlatina, where no communication can be traced with a person previously infected; and we constantly have cases of typhus arising sporadically, where we may fairly consider the patient to have originated the disease within the limits of his own organization.

It is too much the custom to speak of the personal predisposition to infective disorders, as though it consisted in a condition of mere debility. There is no foundation for this view. If we examine cases of pure debility—such as occur under the influence of extreme inanition, or after severe injuries with loss of blood, or towards the close of chronic exhaustive disorders—we do not find in them any marked liability to the infection of morbid poisons generally. In hospital practice, for instance, we do not find that typhus or erysipelas propagates itself among the patients of a ward in proportion to their weakness. It cannot be too distinctly understood that the predispositions to these various disorders are themselves as various as the disorders, and consist in specific conditions of blood, hitherto very imperfectly explored. Mere debility, as such, has nothing directly to do with the matter: a person is liable to the infection of smallpox, because he has one matter in his blood; to that of measles, because he has another; to that of typhus, because he has a third; to that of scarlatina, because he has a fourth, and so on. A predisposition to one of these disorders is by no means necessarily, and possibly not at all, a predisposition to any other of the class. As regards the exterior circumstances which are considered predis-

ponent to infection, I apprehend there can be little question that their mode of operation must for the most part be indirect: that over-crowding and defective ventilation will increase the liability to smallpox or scarlatina only so far as they hinder a natural elimination from the blood of those materials which constitute the liability to the disease, or as they maintain those materials in a state of imperfect oxidation favourable to the zymotic change. In examining the habitations of the poorest classes in our large cities, we find the atmosphere highly animalized—often fetid with organic matters: the air is so little changed, that it stinks with the volatile excretions of the many human beings crowded together; and to these contaminations are very generally added products of decomposition arising from their other excretions which lie in cesspools, or have soaked into the soil beneath and around their dwellings. Such an atmosphere can do little towards purifying the blood of matters wherewith itself is already so loaded: the effete matters of the organism, which naturally seek their elimination in an oxidized state, and which for the healthiest elimination ought probably to be in a high degree of oxidation, are here debarred from completing their discharge in its most normal form; and the inhabitants of such localities are consequently maintained artificially replete with those humoral products which constitute the predisposition to zymotic blood-diseases. It is in these localities, if at all, that such diseases originate *de novo*. I entertain no doubt that some of them do thus originate: though I am unable to state what it is which gives the requisite impetus, or why it is given with one disease oftener than with another. Typhus appears so frequently to arise in this manner, and the predisposition to it is so intimately associated with local circumstances, that some writers have been disposed to overlook the unquestionable evidence that exists of the reproduction and multiplication of the poison in the person of the sufferer, and have inclined to consider it an enchorial disease, incommunicable by personal intercourse.

With respect to other alleged predisponent causes, I incline still more strongly to the view already expressed in regard of atmospheric influences, that they can operate only indirectly, only by means of those specific blood-products which constitute the true predisposition in each case. If fatigue predisposes to a particular infection, it can hardly be for any other reason than that the fatigued organ furnishes the material permissive of infection. If errors or insufficiencies of diet, or certain courses of medicine should be found to form a predisposition to certain infectible disorders, their mode of operation could scarcely be otherwise than by increasing the formation, or diminishing the discharge of that blood-product, which is the immediate object of attack to the zymotic poison.

Therefore, Gentlemen, as respects those instances of human morbid infection with which we are best acquainted, we may recapitulate our facts, and state our theory, in the following terms: that certain materials of the blood—materials not essential to the performance of its nutritive functions, are, by certain circumstances, rendered liable to undergo definite and specific changes; under the

influence of which they become determined, with increased rapidity, to the outlets of the body, and irritate these outlets in their passage; that these changes continue, until the materials affected by them are completely exhausted from the blood; and that the severity and duration of those changes are in proportion to the quantity of material seeking elimination: that the new matters engendered and evolved under these circumstances are capable, in various ways, and with more or less certainty, of producing a precisely similar succession of changes in the blood of another individual, or of any number of individuals; operating always on the same ingredients of the blood as that whence themselves arose, and determining it to the same outlets as that whither themselves were determined; so that the choice of material in the blood, and the choice of outlet in the body, constitute specific characters for the several morbid poisons distinctively, and so that the final products act always as special catalytics for that original material of the blood, wheresoever they may encounter it. But, finally, that under certain possible conditions of accumulation, or tension, in that original material, other circumstances may serve to start it in its progress of specific decomposition, without any demonstrable influence from that exterior catalytic, which is the ordinary occasion of its change.

From our foregone analysis of the pathology of morbid poisons, it is not difficult to deduce philosophical principles of treatment, or to devise a rational explanation of such success and such failure as medicine has hitherto encountered in this department of its ministrations. To check the further conversion of material in the blood; to destroy the poison, or to turn it into harmless combinations; to aid or to anticipate the eliminative efforts of the disease; these would be the indications which pathology would suggest, and these have already, in great part, attained the sanction of experience. But both pathology and practice would concur in adding to these principles another, which, in our present age of palliative medicine, admits of almost infinite application; to remember, namely, that in each zymotic disease, Nature is proceeding in her own way towards a curative termination, and that where (as too commonly happens) we are incompetent to conquer the disease by direct neutralizing antidotes, it behoves us chiefly to devote ourselves to the humbler task of moderating local phenomena, and sustaining constitutional power. Thus it is that, in a vast number of perilous infections, we are able to assist Nature through her difficult process of cure, by no other treatment than the judicious administration of natural, dietetic tonies—food and wine. Thus it is that, while we recognize the absolute efficacy of mercury against the poison of primary syphilis, we constantly find ourselves without an antidote against its later combinations, and confidently rely on measures adopted, without reference to the specific nature of the disease, solely on the ground of their general invigorating power. Till you can neutralize the poison of typhus, of erysipelas, of scarlatina within the blood of your patients, as you would neutralize an acid or an alkali in a test-tube, never lose sight of this important principle; never forget that

these morbid poisons are eminently depressive to life; that they tend to kill by shock and debilitation.

And finally, see what vaccination has done for one of them, formerly, perhaps, the most malignant and unsparing. I have taken pains to explain to you the pathology of its preventive power, and very little reflection on the argument of this lecture will convince you that there is, in the nature of things, no reason why smallpox alone should be frustrated in its tendency—no reason why each zymotic disease should not have its own preventive catalytic—no reason why, in connection with these other pestilences, other men's names should not hereafter be remembered as gratefully and as gloriously as Jenner's in relation to smallpox. Our resources for this great purpose of preventive medicine are not restricted to the teats of cattle. We have the pharmacopœia before us, many of its articles acting catalytically on the blood, and determining products of decomposition, in a characteristic way, to a specific plurality of organs. Not only is there no reason against the possibility that many of these medicinal catalyses may be preventive of the zymotic catalyses; but there is every reason for such a possibility. To give you an illustration—why should not belladonna (determining the products of its operation to the throat, the kidneys, and the skin) act as a medicinal catalytic of that material which constitutes the susceptibility to scarlatina, and thus, in recognized reality (as heretofore in vague tradition), be preventive of that disease? Again, why should not the direct counteractive influence of drugs be extended in respect of these diseases, when they already are in attack? why should we not be enabled by one drug to arrest the blood-change of typhus, and by another that of plague or glanders, just as with quinine we render the blood insusceptible of further detriment from the malarious poison?

These are the directions, Gentlemen, in which it behoves us both to think and to work: and it was because I have a very deep conviction of the importance and future fruitfulness of such studies that, in my last lecture, I dwelt at so much length on the obscure pathology of evacuative medicines. For it is out of large knowledge in pharmacology that successful results will be worked for the aims just indicated to you; and such knowledge, as I have told you, must be of a very different order to those pompous but empty pretensions which at present usurp its place. It must found itself on information, exact and complete, of the several changes which either disease or medicine can produce in the chemistry of the blood and its excretions. From the basis of this information alone, can we pretend to an intelligent application of our resources, or hope to direct our aim, distinctly and efficiently, to those preventive and counteractive purposes which Pathology sets before us.

THE END.